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Introduction: Managing post-transplant COVID-19 patients has proven challenging. On one hand, they are more vulnerable due to their immuno-compromised status, and on the other hand, reducing immunosuppression (IS) may result in graft rejection and formation of de-novo donor specific antibodies (DSA). Here, we share our experience of balancing disease treatment and the risk of rejection in a cohort of renal post-transplant recipients.

Methods: We retrospectively collected data on 136 renal transplant recipients who were diagnosed with COVID-19 between May 2020 and December 2021. Clinical information, demographics and HLA antibody data were extracted from patients’ medical records.

Results: The median time from transplant to COVID-19 diagnosis in our cohort was 4.1 years (range 13 days to 30.8 years). The average age at diagnosis was 50.5 and 63% were males. 29% of the patients were hospitalized and 13.2% had died as a result of their infection. The most common therapies included Monoclonal antibodies (39.7%), Dexamethasone (22%) and Remdesivir (18.4%). IS modulation, which primarily included holding off the anti-metabolite, was done in 98/136 patients (72%), and was later resumed in 70 of the 98 patients with a median time of 8.6 days (range 2-204) from holding off to resuming IS. 25 patients had pre- and post-infection DSA data. Despite the modulation in IS, 23 out of the 25 patients did not show acute rejection. Four patients progressed to graft failure post infection - Two due to worsening chronic antibody mediated rejection, one had not show acute rejection. Four patients progressed to graft failure post infection - Two due to worsening chronic antibody mediated rejection, one had failing graft before COVID-19, suffered a severe disease including intubation and lost his graft shortly after recovering.

Conclusions: Reduction of the anti-metabolic immunosuppressive therapy for a short period of time did not seem to correlate with development of de-novo DSA or increased rates of acute rejection in our expanded cohort. Studies on larger cohorts will help further determine the impact of IS reduction on transplant outcomes following COVID-19 infection in renal transplant recipients.

Immunosuppression Minimization During COVID Infection: Is It Safe?

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Studies on larger cohorts will help further determine the impact of IS reduction during a short period of time did not seem to correlate with development of de-novo DSA, and one had failed graft before COVID-19, suffered a severe disease including intubation and lost his graft shortly after recovering.

Conclusions: Reduction of the anti-metabolic immunosuppressive therapy for a short period of time did not seem to correlate with development of de-novo DSA or increased rates of acute rejection in our expanded cohort. Studies on larger cohorts will help further determine the impact of IS reduction on transplant outcomes following COVID-19 infection in renal transplant recipients.

Impact of mRNA COVID-19 Vaccination on Clinical Outcomes of COVID-19 Infection in Kidney Transplant Recipients at the Singapore General Hospital

Terence Kee1,4, Sobhana D/O Thangaraju1,4, Quan Yao Ho1, Ian Tatt Liew1,4, Jasmine Chung ShinMin2,4, Maslinna Binte Abdul Rahman3, Jin Hua Yong1,4, Nalliee Kwan1,4, Xia He1,4, Eleanor Ng1,4, Limin Wijaya2, Ban Hock Tan2, Michelle Tan Woei Jen1, Thuan Tong Tan2, Chieh Suai Tan1,1.

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Introduction: Since 30th December 2020, Singapore has embarked on an intensive mRNA COVID-19 vaccination program that has resulted in 98% and 70% of its eligible population receiving 2 and 3 doses of mRNA COVID-19 vaccine respectively. However, the impact of mRNA COVID-19 vaccine on outcomes of COVID-19 infection in kidney transplant recipients from Asia remains unknown. This study seeks to determine the impact of mRNA COVID-19 vaccination on clinical outcomes and whether vaccination status can be used as a predictor for good outcomes.

Methodology: Singapore has undergone 4 waves of COVID-19 infection driven by imported cases (2020), outbreaks in foreign worker dormitories (2020), community spread by Delta Variant (2021) and Omicron Variant (2022). During this period, the renal transplant program at SGH set up a COVID-19 registry to prospectively collect data that could be analyzed to guide clinical policies and protocols. Data were analyzed according to number of mRNA vaccine doses given (group A - 3 doses vs. group B - 0 to 2 doses).

Results: Between 22nd June 2020 and 11TH March 2021, 163/864 (18.8%) of kidney transplant recipients followed up at SGH were infected with COVID-19. Among these, 119/163 (73.0%) and 44/163 (26.9%) were in group A and B respectively. Patients in group A were significantly younger (56.1±11.3 vs. 60.4±11.8 years; p=0.03) with a lower 4C Mortality Score (4.5±2.8 vs. 6.0±3.4; p=0.008) but the Charlson Comorbidity Index Score was similar between group A and B (3.5±1.2 vs. 3.8±1.2; p=0.60). Among 155 patients who had anti-SARS CoV2 antibodies (defined as ≥ 500 AU/mL) (44.7%; [n=51/119] vs. 24.4%; [n=11/44]; p=0.07), acute kidney injury occurred less frequently in group A than B (7.6%; [n=9/119] vs. 20.5%; [n=9/44]; p=0.057) but the event rate for intensive care admission (1.7%; [n=2/119] vs. 2.3%; [n=1/44]; p=0.81) and cardiovascular events (2.5%; [n=3/119] vs. 4.5%; [n=2/44]; p=0.669) were low for both group A and B respectively. On multivariate analysis, predictor of oxygen therapy was the 4C Mortality Score (aOR 1.5, 95% CI 1.12-2.02; p=0.001).

Conclusion: Kidney transplant recipients with 3 doses of mRNA COVID-19 vaccine benefited from higher frequency of protective antibody levels. However, it was the 4C Mortality Score that predicted the need for oxygen therapy instead of vaccination status.
210.3

Safe Living Kidney Donor Transplantation During the COVID-19 Pandemic: Experience From the Singapore General Hospital.

Constance Lee1,2, Ping Sing Tee1,2, Xia He1,2, Nicole Leah1,2, Liting Stiew1,2, Sobhana D/O Thangaraju1,2, Quan Yao Ho1,2, Ian Tat Liew1,2, Terence Kee1,2.

1Renal Medicine, Singapore General Hospital, Singapore, Singapore; 2Renal Transplantation, SingHealth Duke-NUS Transplant Center, Singapore, Singapore.

Introduction: In the early period of the COVID-19 Pandemic, many transplant programs in Asia reduced or stopped transplantation activities but later resumed transplantation. In Singapore, living donor transplantation (LKDXT) were suspended for 2 periods (April to June 2020 and May 2021). This study reports on the clinical outcomes of LKDTX performed when transplantation resumed at the Singapore General Hospital. It also report on the effectiveness of peri-transplant protocols to prevent and detect COVID-19 infections in the perioperative period.

Methods: During the COVID-19 Pandemic, all donors and recipients were advised to complete at least 2 doses of COVID-19 mRNA vaccine, adhere to 2 week of social distancing at home before admission for transplant surgery and undertake nasopharyngeal swab for COVID-19 PCR at D-7, D-2 and D-1 prior to LKDTX and weekly thereafter. All donors and recipients were advised to continue social distancing for the first 3 months after transplant surgery and to perform home antigen rapid testing if symptomatic or informed of being a close contact to a COVID-19 infected person. Processes were developed to arrange for infected LKDTX to be directly admitted to COVID-19 wards or receive outpatient SARS-CoV-2 therapeutics with subsequent telemedicine monitoring for 14 to 21 days. Immunosuppression protocols remained unchanged during the Pandemic and high immunological risk kidney transplants with lymphocyte depleting agents and plasma exchange/plasmapheresis proceeded as routine.

Results: A total of 31 LKDXT were performed (10 in 2020 and 21 in 2021), of which 7 (22.6%) were ABO incompatible and 1 (3.2%) were HLA incompatibles, all requiring lymphocyte depleting agents and plasmapheresis. The rates of return to operating theatre, intensive care unit admission, delayed graft function and rejection rate was low at 3.2% (n=1/31), 6.4% (n=2/31), 3.2% (n=1/31) and 6.4% (n=2/31) respectively. Prior to transplantation, no recipient or donor was diagnosed with COVID-19 infection but after transplantation, 6 patients were diagnosed with COVID-19 at a median time of 149 days (range 97 to 386 days) after transplantation, of which all except 1 had received 3 doses of mRNA COVID-19 vaccine. Anti-SARS CoV-2 antibodies were not detected in 50% (n=3/6) and required sotrovimab infusions. Fortunately, the median 4C Mortality Score was 2 (range 2-3) and none of these patients developed pneumonia. Patient and graft survival of all 31 patients remained 100% as of last follow-up.

Conclusions: LKDXT can be performed safely during the COVID-19 Pandemic provided there are protocols set in place for screening donors and recipients for COVID-19 prior to transplantation and during the hospital admission. It is also important for patients to be educated on the importance of home ART surveillance for COVID-19 and to promptly inform the transplant program so that early intervention can be provided to prevent progression to severe COVID-19.

We would like to acknowledge the support of our Head of Department A/Prof Tan Chieh Suai and our hospital's senior management for ensuring resources are made available to continue transplantation activities during the COVID-19 Pandemic.

210.4

Humoral and Cellular SARS-CoV-2 Immunity in Renal Transplant Recipients Following BNT162b2 mRNA Vaccination

Asimina Fyaktou1, Efstratios Kasimatii, Aliki Xochelli1, Anastasia Papadopouloa, Vasilli Nikolas1, Erasmia Sampani2, Despoina Asouchidou1, Maria Stangou2, Evangelia Yannaki3, Georgios Tsoulfas1, Akaterini Papagianni2.

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Introduction: Kidney transplant recipients show poor humoral immune response following SARS-CoV-2 vaccination. Knowledge of vaccine-induced cellular immunity and its association with antibody titers is limited.

Method: SARS-CoV-2–specific neutralizing antibodies (Nab) were measured using chemiluminescence immunoassay in 53 naive kidney transplant recipients after the 2nd dose and before and after the 3rd dose of BNT162b2 mRNA vaccination. Nab were also measured in 23 Covid-19-recovered renal transplant patients before vaccination. Anti-HLA Abs were detected using Luminex to estimate any increase in HLA sensitization after vaccination. In 39 vaccinated patients with no Nab detected after the 2nd dose, SARS-CoV-2–specific  T cells response was studied using interferon (IFN)-γ ELISpot analysis before and one month after the 3rd dose.

Results: One month after the 2nd dose, only 15% of the naive patients demonstrated positive Nab and only 10% preserved them four months later. After the 3rd dose responders increased to 70%, and Nab was preserved in a repeat measurement four months later. Antibody titers after the 3rd dose, had a median value of 9.6 times above the cut-off value; however, they decreased to six times (p=0.003) four months later. Regarding anti-HLA Abs, neither MFI nor HLA specificities increased after vaccination, and none of the patients developed dnDSAs. Of the Covid-19-recovered transplant recipients, 74% demonstrated positive Nab with a median value three times above the cut-off value. In a repeat measurement before vaccination (median time 5 months later), 55% of recovered patients retained their Nab. SARS-CoV-2–specific T cells response was demonstrated in 41% of patients with nonresponse after the 2nd dose. The 3rd dose improved cellular immunity in these transplant recipients, as a specific T cell response was demonstrated in 64% of patients, with a significant increase (p=0.001) in specific T lymphocyte titers.

Conclusion: Vaccination against SARS-CoV-2 appears to be safe regarding the development of anti-HLA Abs in kidney transplant recipients. The humoral immune response improved after the 3rd dose in naive patients, with Nab induced allogeneic to Covid-19-recovered patients, although antibody titers declined four months later. Cellular immunity was present in many patients with primary humoral nonresponse before the 3rd dose and further improved after the 3rd dose, in parallel with Nab induction.
Differential Immunogenicity of mRNA-1273 Versus BNT162b2 as a Third Vaccine Dose for Solid Organ Transplant Recipients Seronegative After Two BNT162b2 Doses.

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Introduction: There is no consensus as to the optimal SARS-CoV-2 vaccination sequence in solid organ transplant recipients (SOTRs). Anti-spike antibody response to the two-dose BNT162b2 mRNA vaccine series is poor in SOTRs, and it is possible that the higher-dose mRNA-1273 vaccine could improve immunogenicity in suboptimal responders, who are at high risk for SARS-CoV-2 infection.

Methods: We evaluated 114 SOTRs who tested negative on an anti-spike antibody assay after two doses of BNT162b2 and had a third dose (D3) of either homologous BNT162b2 or heterologous mRNA-1273 vaccine. The proportion of seroconversion at 1 month post-D3 was compared between groups using Fisher’s exact testing. Additionally, the rate of high-titer response at 1 month post-D3, defined as achieving an antibody level associated with neutralizing capacity versus the ancestral SARS-CoV-2 variant (≥250 binding antibody units), was analyzed using multivariable Poisson regression with robust standard error, adjusting for mycophenolate (MMF) use, age, and years since transplant.

Results: Overall, 99 SOTRs received homologous BNT162b2 D3 and 15 received heterologous mRNA-1273 D3. There was no significant difference in age (median 65 [IQR 50-71] vs 63 [58-68] years), sex (59% vs 69% female), time since transplant (median 4 [IQR 2-10] vs 7 [2-15] years), or MMF use (84% vs 80%) between BNT162b2 and mRNA-1273 D3 groups, though calcineurin inhibitor use differed (88% vs 67%, p=0.03). Seroconversion at 1 month post-D3 was similar between BNT162b2 and mRNA-1273 D3 groups, though calcineurin inhibitor use differed (88% vs 67%, p=0.03). Seroconversion at 1 month post-D3 was similar between BNT162b2 and mRNA-1273 D3 groups, though calcineurin inhibitor use differed (88% vs 67%, p=0.03). Seroconversion at 1 month post-D3 was similar between BNT162b2 and mRNA-1273 D3 groups, though calcineurin inhibitor use differed (88% vs 67%, p=0.03). Seroconversion at 1 month post-D3 was similar between BNT162b2 and mRNA-1273 D3 groups, though calcineurin inhibitor use differed (88% vs 67%, p=0.03). Serocconversion at 1 month post-D3 was similar between BNT162b2 and mRNA-1273 D3 groups, though calcineurin inhibitor use differed (88% vs 67%, p=0.03). Serocconversion at 1 month post-D3 was similar between BNT162b2 and mRNA-1273 D3 groups, though calcineurin inhibitor use differed (88% vs 67%, p=0.03).

Conclusion: In SOTRs without initial response to two-dose BNT162b2 vaccination, a heterologous mRNA-1273 D3 showed similar serocconversion rates (~50%) to homologous BNT162b2 D3, but was significantly more likely to generate high-titer responses. Further directions include assessment of COVID-19 breakthroughs among vaccine regimens, as well as exploring the neutralizing capacity and durability of antibody response to heterologous platforms.

Table 1: Clinical and transplant characteristics of solid organ transplant recipients testing seronegative after two-dose BNT162b2 series, by type of third vaccine received. Categorical and continuous outcomes were analyzed using Fisher’s exact and Wilcoxon rank-sum test respectively.

<table>
<thead>
<tr>
<th></th>
<th>Homologous BNT162b2 n=99</th>
<th>Heterologous mRNA1273 n=15</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>age, median [IQR]</td>
<td>65 [50, 71]</td>
<td>63 [58, 68]</td>
<td>0.91</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>56 [59]</td>
<td>9 [69]</td>
<td>0.56</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>9 (9)</td>
<td>17 (17)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Allergic, n (%)</td>
<td>54 (55)</td>
<td>12 (80)</td>
<td>0.16</td>
</tr>
<tr>
<td>Kidney</td>
<td>15 (15)</td>
<td>1 (7)</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>17 (17)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>10 (10)</td>
<td>1 (7)</td>
<td></td>
</tr>
<tr>
<td>Kidney &amp; Liver</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Kidney &amp; Other ( unspecified)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Liver &amp; Heart</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Heart &amp; Lung</td>
<td>0 (0)</td>
<td>1 (7)</td>
<td></td>
</tr>
<tr>
<td>Years since transplant, median [IQR]</td>
<td>4 [2, 10]</td>
<td>7 [2, 15]</td>
<td>0.15</td>
</tr>
<tr>
<td>Calciuminhibitor, n (%)</td>
<td>87 (88)</td>
<td>10 (77)</td>
<td>0.032</td>
</tr>
<tr>
<td>Anti-metabolite, n (%)</td>
<td>85 (86)</td>
<td>13 (87)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Steroids, n (%)</td>
<td>59 (60)</td>
<td>11 (73)</td>
<td>0.31</td>
</tr>
<tr>
<td>Triple I: steroids, CDI, antimetabolite, n (%)</td>
<td>46 (46)</td>
<td>7 (47)</td>
<td>0.99</td>
</tr>
<tr>
<td>Days between D2 and D3 vaccine, median [IQR]</td>
<td>170 (146, 187)</td>
<td>151 (107, 177)</td>
<td>0.058</td>
</tr>
<tr>
<td>Anti-RBD serostatus 1 month post-D3, n (%)</td>
<td>29 (22, 32)</td>
<td>31 (28, 32)</td>
<td>0.39</td>
</tr>
<tr>
<td>Negative</td>
<td>48 (48)</td>
<td>7 (47)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>53 (53)</td>
<td>8 (53)</td>
<td></td>
</tr>
<tr>
<td>High-titer anti-RBD level 1 month post-D3 (RBD &gt;=250 U/mL), n (%)</td>
<td>82 (83)</td>
<td>8 (53)</td>
<td>0.016</td>
</tr>
<tr>
<td>Negative or low level</td>
<td>0.83</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td>High-titer</td>
<td>17 (17)</td>
<td>7 (47)</td>
<td></td>
</tr>
</tbody>
</table>

ASTS Jon Fryer Resident Scientist Award. National Institute of Diabetes and Digestive and Kidney Diseases: T32DK007732 (Dr. Chang), T32DK007713 (Dr. Alejo), K01DK101677 (Dr. Massie), K01DK114388-03 (Dr. Levan), and K23DK115908 (Dr. Garonzik-Wang). National Institute of Allergy and Infectious Disease: K23AI157893 and U01AI136897 (Dr. Werbel) and K24AI144954 (Dr. Segev).
COVID-19 Positive Donor Organs in Transplantation

Vijay Subramanian1, Rachel Hogen1, Diego Reino1, Benjamin Mackie2, Lucian Lozonschi2, Kiran Dhanireddy1, 1Transplant Institute, Tampa General Hospital, Tampa, FL, United States; 2Department of Cardiothoracic Surgery, University of South Florida, Tampa, FL, United States.

Introduction: Due to unknown transmission risks, donors with acute COVID-19 infection manifested by positive PCR test were ineligible for organ donation in the past. We report our experience with 6 donors with acute COVID-19 infection whose organs were used for transplantation.

Methods: Retrospective review of outcomes of transplantation from COVID-19 positive donors.

Results: Organs from six brain dead donors were utilized for transplantation. Donors were tested with COVID-19 PCR either on nasopharyngeal swabs or Bronchoalveolar lavage specimens or both. Heart, liver and kidney were used for transplant from 1 donor, heart was utilized from 2 and liver from 3 of the donors. Three donors had discrepancy in results with a negative nasopharyngeal PCR, but positive BAL specimen. One donor had symptomatic COVID-19 infection (pneumonia) and all others were asymptomatic. Cycle threshold was >25. Recipients included 3 heart transplant, 3 liver transplant and 1 combined liver-kidney transplant. All recipients had completed full vaccination series, and three received additional post transplant pre-exposure prophylaxis with Tixagevimab/Cilgavimab. Standard post transplant immunosuppression with steroids, CNI and antimetabolite was used. Two heart transplant recipients underwent post transplant treatment for AMR. There were no post transplant COVID infections with median follow up of 40 days. All patients and grafts are doing well.

Conclusion: Successful transplantation of organs from donors with COVID-19 infection is feasible. Appropriate donor and recipient selection and risk assessment is essential and long term follow up to rule out any transmittable risks of donor derived infection.


 Haley Hardgrave1, Joe Nigh2, Sushma Bhusal3, Lyle Burdine4, Raj Patel5, Emmanouil Giorgakis6

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Introduction: With one-third of the United States still not fully vaccinated for COVID-19 and almost one-half unvaccinated in Arkansas, it is common to see patients presenting with non-survivable diagnosis, incidentally testing COVID-19+ or with recent history of mild COVID-19 infection. In the absence of COVID-19, such patients could become organ donors. Limited case series have demonstrated no COVID-19 syndrome following transplantation from such donors. However, hematogenous asymptomatic transmission of the COVID-19 virus following transplant remains unclear. Aim of this study was to assess COVID-19 virus presence in the recipient’s bloodstream at the early post-transplant period following COVID-19+ organ transplantation.

Methods: An institutional protocol was drafted for the use of COVID-19+ donor organs. Eligible donors included those test COVID-19+, however with cause of death not related to COVID-19, and no evidence of moderate to severe COVID-19. Eligible recipients included those who tested negative for COVID-19 at the time of transplant, had been fully vaccinated against COVID-19, and consented to receive such organs. A protocol deviation occurred when a COVID-19+ organ was transplanted into a non-vaccinated recipient with recent history of resolved COVID-19 infection. Plasma was drawn to test for COVID-19 polymerase chain reaction (PCR) prior to hospital discharge post-transplant. All recipients received tixagevimab-cilgavimab (Evusheld) after plasma COVID-19 PCR testing.

Results: Six recipients underwent kidney transplantation from COVID-19+ donors. One donor had reported mild symptoms of COVID-19 prior to hospitalization. Two donors tested Hepatitis C positive by nucleic amplification testing. 83.3% (N=5) of recipients were fully vaccinated prior to transplant (Table 1). An additional recipient had not been vaccinated but had history of recent COVID-19 infection. None of the recipients developed COVID-19 symptoms post-transplant. All had undetectable serum plasma COVID-19 PCR prior to discharge (testing range post-operative day 2 to 5). Post-transplant median length of stay was 3 days. Median follow-up was 39 days (33, 62). Two recipients had delayed renal allograft function. One patient developed antibody-mediated rejection diagnosed on post-operative day 30. No recipients required post-transplant testing for suspected COVID-19 symptoms. There was no mortality (Table 2).

Discussion: This case series provides proof of concept that there is no evidence of hematogenous transfer of COVID-19 from donor positive organs to recipients immune to the virus. Therefore, otherwise transplantable organs from donors incidentally diagnosed with COVID-19 at the time of donation, with no indication of severe COVID-19 disease at the time of donation, should be considered for non-thoracic organ transplantation to suitable recipients, after appropriate consenting.
Abstracts

210.8
Timely Lower Respiratory SARS-CoV-2 Testing of All Potential Organ Donors Leads to Successful Transplantation of Organs From SARS-CoV-2+ Donors

Christine Radolovic1, Sharon West1, John Edwards1, Richard D Hasz1.
1Gift of Life Donor Program, Philadelphia, PA, United States.

Introduction: Early on in the pandemic, COVID-19 was a rule-out for organ donation. The development of protocols to best screen potential organ donors was necessary to continue to provide life-saving organ transplants while minimizing the risks of COVID-19 transmission.

Method: This was a single OPO, multi-center observational study. The OPO initiated SARS-CoV-2 testing by lower respiratory (tracheal aspirate) specimens for all potential deceased organ donors and worked with 2 local labs that together could perform testing 24 hours a day and return results including Cycle Threshold (CT) within approximately 6 hours.

Results: Between 1/1/2021 and 2/28/2022, 572 (8.7%) of the 6570 ventilator-dependent patients with non-survivable neurological injuries referred to the OPO tested positive for SARS-CoV-2 by upper respiratory specimen (typically performed by the referring hospital lab) or by lower respiratory specimen (performed by the OPO affiliated lab). Of the 572 COVID+ patients, 480 were determined to be medically unsuitable and in 42 cases the NOK declined organ donation. Of the 57 patients that went on to become organ donors, the CT ranged from 16.3 to 43.1, and 78 kidneys, 34 livers, 11 hearts and 2 pancreas were transplanted at 38 transplant centers. No suspected transplant related disease transmissions were reported.

Conclusion: Continued referral and assessment of all potential organ donors throughout the pandemic regardless of SARS-CoV-2 infection status, along with improved and timely access to lower respiratory testing including CT results led to the successful utilization of organs from COVID-19+ donors for transplant.

Table 1. Donor and Recipient Demographics

<table>
<thead>
<tr>
<th>Donor (N=5)</th>
<th>N (%)</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>5.0 (100)</td>
</tr>
<tr>
<td>DBD Procurement</td>
<td>2.0 (40.0)</td>
</tr>
<tr>
<td>DCD Procurement</td>
<td>3.0 (60.0)</td>
</tr>
<tr>
<td>Reported COVID-19 Symptoms</td>
<td>1.0 (20.0)</td>
</tr>
<tr>
<td>Hepatitis C Positive</td>
<td>2.0 (40.0)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>Age (Years) 47.0 (38.0, 51.0)</td>
</tr>
<tr>
<td></td>
<td>KDPI 65.0 (61.0, 66.0)</td>
</tr>
<tr>
<td></td>
<td>CIT (Hours)* 23.3 (20.7, 24.4)</td>
</tr>
<tr>
<td></td>
<td>WIT (Minutes, DCD only) 11.0 (10.5, 16.6)</td>
</tr>
<tr>
<td>Recipient (N=6)</td>
<td>N (%)</td>
</tr>
<tr>
<td></td>
<td>Full Vaccination** 5.0 (83.3)</td>
</tr>
<tr>
<td></td>
<td>Prior COVID-19 Infection (within 6 months) 1.0 (16.7)</td>
</tr>
<tr>
<td></td>
<td>Diabetes Mellitus 3.0 (50.0)</td>
</tr>
<tr>
<td></td>
<td>Hypertension 3.0 (50.0)</td>
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<tr>
<td></td>
<td>On dialysis 5.0 (83.3)</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
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<td></td>
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</tbody>
</table>

Table 2. Transplant Outcomes

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Positive COVID-19 Plasma PCR 0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Post-transplant COVID-19 Symptoms 0</td>
</tr>
<tr>
<td></td>
<td>ICU Admission 0</td>
</tr>
<tr>
<td></td>
<td>28-Day Rejection 0</td>
</tr>
<tr>
<td></td>
<td>28-Day Mortality 0</td>
</tr>
<tr>
<td></td>
<td>Median (IQR)</td>
</tr>
<tr>
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</tr>
</tbody>
</table>

ICU: Intensive Care Unit
PCR: Polymerase Chain Reaction
The High Incidence of Long-COVID-19 in Kidney Transplant Recipients: A Longitudinal Cohort Study

Vinicius Lafico1, Helio Tedesco-Silva1, José Medina-Pestana1, Carlos Amorim2, Marina Cristelli1.

1Nephrology, Hospital do Rim, Sao Paulo, Brazil; 2Physical Education, Federal University of Maranhão, São Luís, Brazil.

Purpose: This study aimed to investigate the clinical consequences of three months after symptom onset among kidney transplant recipients surviving COVID-19.

Methods: This is an ongoing single-center observational prospective study that includes adult kidney transplant recipients diagnosed and followed after COVID-19 between 03/20/2020 and 05/31/2021. Patients who lost their graft were excluded. The patients will receive a telephone at 3, 6, and 12 months after symptom onset from the clinical research team. The call consisted of a structured symptoms questionnaire with binary answers (yes/no). The questionnaire included the following symptoms: headache, dizziness, anosmia/ageusia, weakness, myalgia, inappetence, diarrhea, and dyspnea, which could be presented before and/or after the COVID-19 diagnosis. Those patients with at least one symptom showed just after the disease was defined as having Long-COVID-19. Subsequently, the clinical research team included a question about the work status. Adjusted multivariable logistic regression models were used to identify the risk factors associated with Long-COVID-19.

Results: There were 1,731 patients with COVID-19, with 455 deaths and 36 graft losses. Of the remaining 1,240 patients, 454 (36%) didn’t answer our calls, yielding a final cohort of 786 patients. Of them, 217 (28%) developed Long-COVID-19. The incidence of each symptom at three months was: dyspnea (7%), myalgia (12%), weakness (11%), headache (10%), dizziness (7%), diarrhea (4%), inappetence (4%) and anosmia/ageusia (3%). About 1% of our patients needed domiciliary O2. Of those who obtained the functional status (n=239), 95 (40%) were employed before COVID-19, and 79 of them (7%) had returned to their original work at three months. After COVID-19 diagnosis, 44% of the patients were hospitalized (31% in ICU), 35% used supplemental O2, and 5% required mechanical ventilation. Fever (53%), shiver (39%), nausea (3%), anosmia/ageusia (59%), hospitalization (67%), and adverse cardiovascular events (3%), such as thrombosis or myocardial infarction, were risk factors associated with subsequent development of Long-COVID-19, using adjusted multivariable logistic regression.

Conclusion: The incidence of Long-COVID-19 at three months was 28% and was associated with reduced quality of life and return to work. Several COVID-19 associated symptoms and disease severity markers were associated with Long-COVID-19.

Seroconversion After Vaccination With BNT162b2 Pfizer/BioNTech, ChAdOx1 nCoV-19/AZD1222 and Coronavac Against Sars-cov-2 Among Hemodialysis and Kidney Transplant Patients

Alfredo Chew-Wong1, Lizbeth Morales-López1, Elizabeth Hernández-Infante1, José M. Areolla Guerra1, Guadalupe Ricalde-Ríos1, Isis A. Velázquez-Ramírez1, Luis Romo-Franco1, Ana B Lagunas-Rodríguez1, Mario González-Gámez1, Rafael Reyes-Acevedo1.

1Nephrology and Kidney Transplantation, Centenario Hospital Miguel Hidalgo, Aguascalientes, Mexico.

Background: Since December 2019 the world has been affected by the SARS-CoV2 pandemic. In the state of Aguascalientes, Mexico, at least 62,400 cases and 3,479 deaths due to COVID-19 have been confirmed so far. As an strategy against SARS-CoV-2, many vaccines have been developed, from which only BNT162b2 Pfizer/BioNTech, ChAdOx1 nCoV-19/AZD1222 and CoronaVac are available at our state. It has been shown that patients on dialysis and renal transplantation have a high morbidity and mortality due to COVID-19.

Objective: To assess and compare the seroconversion level (≥100U/mL) in patients with chronic kidney disease on hemodialysis (HD) and kidney transplant recipients (KTR), who received two doses of the BNT162b2 Pfizer/BioNTech, ChAdOx1 nCoV-19/AZD1222 and CoronaVac vaccines. To identify the risk factors associated with a suboptimal response of the vaccine received in our study population.

Methods: We conducted a prospective, observational, non-blind, comparative study, which included adult patients from age 18 to 80 years, both genres, undergoing renal replacement therapy with hemodialysis or kidney transplantation, who had received two doses from the BNT162b2 Pfizer/BioNTech, ChAdOx1 nCoV-19/AZD1222 and CoronaVac vaccines. To identify the risk factors associated with a suboptimal response of the vaccine received in our study population.

Results: One hundred and thirty-three patients were included, 99 of them were undergoing HD and 32 were KTR. The multiple logistic regression analysis used the seroconversion ≥100U/mL as a dependent variable, determined using the Elecsys anti-SARS-CoV-2 immunoassay.

Statistical analysis: Chi-square test with Yates correction, non-paired Statistical analysis: We conducted a prospective, observational, non-blind, comparative study, which included adult patients from age 18 to 80 years, both genres, undergoing renal replacement therapy with hemodialysis or kidney transplantation, who had received two doses from the BNT162b2 Pfizer/BioNTech, ChAdOx1 nCoV-19/AZD1222 and CoronaVac vaccines. To identify the risk factors associated with a suboptimal response of the vaccine received in our study population.

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Results: One hundred and thirty-three patients were included, 99 of them were undergoing HD and 32 were KTR. The multiple logistic regression analysis used the seroconversion ≥100U/mL as a dependent variable, determined using the Elecsys anti-SARS-CoV-2 immunoassay.

Conclusion: Renal replacement therapy with HD was associated with a greater frequency of seroconversion, independently of the type of vaccine received, compared to the kidney transplant receptors. Patients with a kidney transplant exhibited a greater frequency of SARS-CoV2 infection after the vaccination, compared to the patients undergoing HD. Kidney transplantation was the main risk factor associated to a smaller rate of conversion, regardless of the type of vaccine.

Akhay Khatri¹, Jacques Simkins¹,², Neeraj Sinha³, Anita Phancao², Gsetian Ciancio², Lilian M. Abbo¹,², Giselle Guerria, Yoichiro Natori¹,², Shweta Anjja³,¹
¹Department of Medicine, Division of Infectious Disease, University of Miami Miller School of Medicine, Miami, FL, United States; ²Miami Transplant Institute, Jackson Health System, Miami, FL, United States;

Introduction: During the ongoing Coronavirus disease 2019 (COVID-19) pandemic, there have been increasing reports of co-infections with viral, bacterial and fungal pathogens. Two specific COVID-19-related fungal infections have been identified – COVID-19 associated pulmonary aspergillosis (CAPA) and COVID-19 associated mucormycosis (CAM), with limited information available about their incidence and occurrence in solid organ transplant recipients (SOTRs). We describe our experience with COVID-19 associated fungal co-infections (CFIs) in SOTRs with COVID-19.

Methods: This was a single center retrospective study at a large volume transplant center in South Florida, USA. We included adult SOTRs (≥18 years) diagnosed with COVID-19 between March 1st 2020 and January 31st 2022, with a subsequent diagnosis of CFI. We collected information related to demographics, comorbidities, COVID-19 diagnosis and therapeutics, and CFI diagnostics and management. We performed descriptive statistical analysis on the data obtained.

Results: We identified 612 SOTRs with COVID-19, of which 23 (3.8%) were diagnosed with CFI and role for anti-fungal prophylaxis.

Conclusions: We found that solid organ transplant patients, the CDC recommends a primary series vaccination with inactivated SARS-CoV-2 vaccine (CoronaVac, Sinovac) or BNT162b2 mRNA vaccine (Comirnaty, Pfizer-BioNTech) in this high-risk population.

Introduction: Vaccination against SARS-CoV-2 reduces COVID-19 mortality and complications in solid organ transplant recipients. We evaluated the associated antibody responses and breakthrough infections following vaccination with inactivated SARS-CoV-2 vaccine (CoronaVac, Sinovac) or BNT162b2 mRNA vaccine (Comirnaty, Pfizer-BioNTech) in this high-risk population.

Method: This prospective observational study (April 2021-February 2022) included 10 liver and 38 kidney transplant recipients who received 2 vaccine doses (Sinovac, n = 31; or BioNTech, n = 17) as primary series all of whom provided blood samples (4-6 weeks after second dose) for quantitative antibody tests (Abbott Quant assay for immunoglobulin G antibodies against SARS-CoV-2 spike protein). Following the end of the primary series, all patients were monitored for the development of infection for 9 months. The booster doses given to the patients throughout the follow-up were also documented. Type I error was α = 0.05 in all statistical analyses (SPSS, version 25).

Results: We analyzed demographic data, antibody responses after 2 doses of SARS-CoV-2 vaccine as primary series, booster doses and development of breakthrough infection. Median age was 36.5 and 35 (73%) of them were male. Five patients developed COVID-19 in the first six months after the primary series were completed, four of them had received two doses of Sinovac and one had received two doses of BioNTech. Only one patient had needed hospitalization vaccinated with two doses of Sinovac and her antibody level was 0 AU/mL. The median antibody level in patients who developed COVID-19 was 41.9 AU/mL, while it was 312.0 AU/mL in those who did not. However the difference was not statistically significant (p=0.092). Between the 6th and 9th months, 11 participants tested positive for SARS-CoV-2 PCR, with all isolates being Omicron variant. While the rate of positivity was 17% in patients who had at least two booster doses of mRNA vaccine after two consecutive doses of primary series, it was 27% in patients who received just one dose or no booster.

Conclusion: Solid-organ transplant recipients demonstrated inadequate vaccine responses. In addition, with the decrease in the immune response developed with the vaccine over time, it is seen that the newly emerged variants significantly increase the need for additional doses. In solid organ transplant patients, the CDC recommends a primary series of three doses at one-month intervals with a booster dose three months later. Despite the small amount of data, the findings of our study support this requirement.
Humoral Response to SARS-CoV-2 Vaccination in Kidney Transplant Recipients

Maria Butiu, Bogdan Obrisca, Lena Sibulesky, Ramasamy Balthavatsalam, Kelly D. Smith, Idoia Gimferrer, Gener Ismail, Nicolae Leca.

Division of Nephrology, University of Washington, Seattle, WA, United States; Department of Nephrology, Fundeni Clinical Institute, Bucharest, Romania; Division of Transplant Surgery, University of Washington, Seattle, WA, United States; Department of Laboratory Medicine and Pathology, University of Washington, Seattle, WA, United States; Immunogenetics/HLA Laboratory, Bloodworks Northwest, Seattle, WA, United States.

Introduction: We sought to evaluate the humoral response to SARS-CoV-2 vaccination in a cohort of kidney transplant (KT) recipients and to identify factors associated with poor humoral immune response.

Method: Serum samples collected from COVID-19 vaccinated kidney transplant (KT) recipients from 3/1/21 to 4/26/21 were tested for COVID-19 antibodies using a novel multi-antigen detection Luminex platform (BioRad). We measured the specific anti-SARS-CoV-2 IgG antibodies against the individual components of the trimeric spike protein, namely spike 1 (S1), spike 2 (S2) and receptor-binding domains (RBDs). In addition, documentation of previous infection was assessed by measuring anti-nucleocapsid antibodies.

Results: The study cohort enrolled 104 KT recipients that underwent assessment of serological responses at a median 3 weeks (IQR: 1.6-4.9) after vaccination. The majority of patients received either the BNT162b2 (50%) or mRNA-1273 (47.1%), with only 2.9% of patients receiving the Ad26.COV2.S vaccine. Overall, 32.7% of patients became seropositive with a median anti-S1 IgG and anti-RBD IgG levels of 403 BAU/ml (IQR: 82-800) and 206 BAU/ml (IQR: 41-800). In terms of predictive factors for vaccine response, we identified that those on an immunosuppressive regimen containing MMF were less likely to develop a seroconversion (relative risk [RR], 0.54 [95% CI, 0.31-0.94]; p=0.03). By contrast, patients with evidence of previous infection as documented by anti-nucleocapsid positivity were significantly more likely to became seropositive (RR, 2.73; 95%CI, 1.7-4.39; p<0.001). Regarding the temporal evolution of humoral response, there is a clear tendency for a weaning of antibody response over time. In patients with a vaccine response, the median titer of anti-RBD antibodies decreased from 800 BAU/ml (IQR: 257-800), in patients with serum samples taken within 2 weeks after vaccination, to 168 BAU/ml (IQR: 64-41), in patients with samples taken after more than 4 weeks post vaccination (p=0.15). Similarly, the anti-S1 IgG antibody titers were higher in patients with serum samples taken early after vaccination (IQR: 876-700), for 0-2 weeks; 579 BAU/ml (IQR: 39-800), for 2-4 weeks and 97 BAU/ml (IQR: 37-251) for > 4 weeks (p=0.05). In multivariate logistic regression analysis, we identified the presence of anti-nucleocapsid IgG antibodies as being independently associated with approximately 8-fold higher chance for a seroconversion (HR, 7.96; 95%CI, 1.26-50.1), while use of MMF-containing immunosuppressive regimens decreased the chance of humoral response by approximately 66% (HR, 0.34; 95%CI, 0.1-1.11).

Conclusion: Kidney transplant recipients have a poor humoral immune response to a two-dose regimen of SARS-CoV-2 vaccine. Previous natural infection increase the likelihood for development a seroconversion, while MMF-containing regimens decreased vaccine responsiveness.
Humoral Response to COVID-19 mRNA Vaccines in a Cohort of Young Kidney Transplant Recipients From a Single Center in Northern Italy

Marco Cazzaniga1, Sara Testa2, Olga Caporale2, Maria Viganoni3, Giovanni Montini4.
1IRCCS Ca’ Granda Osp Maggiore Policlinico - Pediatric Nephrology, Dialysis and Transplantation Unit, University of Milan, Milano, Italy; 2Pediatric Nephrology, Dialysis and Transplantation Unit, Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milano, Italy.

Objective: To investigate immune-response to COVID-19 vaccines in young kidney transplant (KT) recipients from Northern Italy.

Methods: We prospectively studied KT patients aged 12-25 years, managed in our Center on maintenance IS therapy (corticosteroids, CNI and anti-proliferative agents), eligible for antiSARS-CoV-2 vaccination according to the schedule of the Italian Medicines Agency for immunosuppressed patients (two doses plus additional dose one month later). From 1 July 2021 to 28th February 2022 we evaluated antiSpike-protein antibody response at T0 (before vaccine), T1, T2 and T3 (14±3 days after 2nd and 3rd dose and 90±7 days after 3rd dose, respectively) to BNT162b2 (Pfizer/BioNTech) or mRNA-1273 (Moderna). AntiSpike total lg titer cut-off was 0.8 U/ml (Roche® Elecsys Anti-SARS-CoV-2-S). Exclusion criteria: KT or additional IS within 6 months, relapse of primary disease, vaccine before KT, ongoing COVID-19, patients resident outside the Region.

Results: Eighty-seven patients were eligible; 68 patients were enrolled. Median age: 19.5 (IQR:16.3-21.9) years; median time from KT: 61.4 (IQR:36.7-111.7) months. Five patients dropped out of study after enrolment. Anti-SARS-CoV2 Spike Antibodies response to mRNA vaccines is shown in Figure 1; 90% of non-responders at T1 (20 patients) seroconverted at T3. We didn’t find correlation between time from KT (the shorter time, the most response) and Ig-titer. Twelve out of 58 pts developed COVID19 after the third additional vaccine dose; in this population AntiSpike lg titer at T2 was lower compared to the value of non infected patients, even if not statistically significant: 144 U/ml (IQR:9.4-3683) vs. 4771 U/ml (IQR:79.1-111.7) months. Five patients dropped out of study after enrollment.

Conclusions: KT pediatric recipients exhibit a satisfactory response after 2 doses of vaccine, that become comparable to that of immunocompetent population after the third. Furthermore, the response after two doses is better if compared with adult KT population (63.6% vs 44.8%).

Figure 1: Anti-SARS-CoV2 Spike Antibodies response to mRNA vaccines

MRNA Based Vaccines Against SARS-CoV-2 Do Not Alter cPRA in Patients Awaiting Kidney Transplant

Miko Rewinski2,3, Pamela Doyle2,3, Daniel Durkin2,3, Sandy Vick2,3, Joseph Devivo2,3, Roger Caruk2,3, Andrew Haberman1, Debera Palmeri1, Pamela Cry1, Glyn Morgan1,2,3,4, Oscar Serrano1,2,3,4, Bishoy Emmanuel1,2,3,4, Zeynep Ebioglou1,3,5, Joseph U Singh1,2,3,5, Rebecca Kent1,2,3,5, Xiaoyi Yo1,2, Joseph Tremaglio3,5, Laurine Bow1,2,3,6, Wasim Dar1,2,3,4,1Surgery, Hartford Hospital, Hartford, CT, United States; 2Transplant and Comprehensive Liver Center, Hartford Hospital, Hartford, CT, United States; 3HLA Lab, Hartford Hospital, Hartford, CT, United States; 4Surgery, University of Connecticut School of Medicine, Farmington, CT, United States; 5Medicine, University of Connecticut School of Medicine, Farmington, CT, United States; 6Surgery, Yale University School of Medicine, New Haven, CT, United States.

Introduction: A recent case report in a patient awaiting living donor kidney transplant demonstrated vaccination against SARS-CoV-2 with resulted in B-cell activation causing emergence of DSA. This raises the questions as to whether vaccination against SARS-CoV-2 should be considered a sensitizing event and warrant increased testing of sera for anti-HLA antibodies in patients awaiting kidney transplant.

Methods: We sought to anwer this question by reviewing anti-HLA antibody testing results in sensitized and unsensitized patients before and after vaccination against SARS-CoV-2. Patients were selected on the basis of having received at least two doses of either the Pfizer or Moderna SARS-CoV-2 vaccine and have sera tested before and after receiving the vaccinations. 12 sensitized and 10 unsensitized who met criteria were indentified. Sera was tested using Luminex single antigen bead platforms per protocol. Results included anti-HLA antibody specificity as well as MFI ranges. cPRA was calculated from these values.

Results: In 11/12 sensitized patients vaccination against SARS-CoV-2 did not result in production of new anti-HLA antibodies nor appreciably change the MFI of existing antibodies. One sensitized patient did have an increased number of both class I and class II antibodies after vaccination but this patient also stopped immunsuppression prior to receiving the vaccine. Thus this patient’s results are likely attributable to alterations in immunosuppression and not from vaccination (Figure 1). In unsensitized patients, there was no de novo development of anti-HLA antibodies after vaccination.

Conclusion: Vaccination against SARS-CoV-2 did not result in de novo development of anti-HLA antibodies in unsensitized patients and did not alter the specificity nor the MFI’s of existing anti-HLA antibodies in sensitized patients. This indicates that there is no broad need for increased testing of sera in patients awaiting kidney transplant after SARS-CoV-2 vaccination.
Antibody Response to Booster mRNA COVID-19 Vaccine After Standard Doses of Various Homologous and Heterologous Vaccines in Kidney Transplant Recipients

Ahram Han1, Sangil Min1, Eun-Ah Jo1, Hye young Woo1, Ara Cho1, Hajoong Lee2, Yong Chul Kim2, Hee Kyung Kang3, Yo Han Ahn3, Eun Young Song4, Jongwon Ha1.
1Department of Surgery, Seoul National University College of Medicine, Seoul, Korea; 2Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea; 3Department of Pediatrics, Seoul National University Children’s Hospital, Seoul, Korea; 4Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Korea.

The immune response to standard doses of COVID-19 vaccines in kidney transplant recipients (KTRs) is suboptimal and additional doses are being recommended. The type of COVID-19 vaccine one had access to during the initial standard doses of vaccination was largely dependent on its availability. Thus some had homologous vaccines (i.e. 2 doses of viral vector vaccine or 2 doses of mRNA vaccine) and others had heterologous vaccines during the initial standard vaccination. The effect of such different vaccine combinations on the effectiveness of booster shots using mRNA vaccines in KTRs is largely unknown. The current study is a noninterventional prospective study examining the efficacy of the additional dosage of the COVID-19 vaccine in KTRs. Patients with standard doses of COVID-19 vaccines were enrolled. Reactogenicity to COVID-19 was assessed two weeks before and one month after the additional dose (booster shot) by examining anti-SARS-CoV-2 IgG antibodies against the receptor-binding domain of the S1 subunit of the spike protein using SARS-CoV-2 IgG II Quant assay (Abbott). A total of 235 KTRs with standard doses of COVID-19 vaccine were enrolled. During the initial vaccination, 106 (45.1%) had two doses of mRNA vaccine (BNT162b2 or mRNA-1273), 73 had ChAdOX1-S/ BNT162b2 52 (22.1%) had ChAdOX1-S/ ChAdOX1-S, and one (0.4%) had Janssen COVID-19 vaccine. All patients had mRNA vaccines (BNT162b2 or mRNA-1273) for booster. After the booster dose, seropositivity improved from 55.3% (130/235) to 81.3% (191/235) with seroconversion in 58.1% (61/105) of the initially seronegative patients. Antibody titer also was significantly increased (median, 62.3 to 1382.8 AU/mL, p<0.01 by Wilcoxon rank sum test).

Risk factors for negative antibody response to booster mRNA were low eGFR (OR 0.95, 95% CI 0.93-0.98) and having two doses of viral vector vaccines during the standard vaccination (OR 5.43, 95%CI 1.59-18.49; reference-mRNA/mRNA vaccine). This was likely due to the relatively low immunity before the third vaccine dose within this patient group (negative response in 69.2%). The use of an additional dose of COVID-19 mRNA vaccine is effective in eliciting antibody response in KTRs, especially for those in whom the primary vaccination failed. Overall response after an additional dose of mRNA vaccine was affected by the type of vaccines used during the standard vaccination.

### Table: Antibody Response to Booster mRNA COVID-19 Vaccine

<table>
<thead>
<tr>
<th>DOB</th>
<th>PRA</th>
<th>Vaccine Pre-Vaccine OPRA</th>
<th>Vaccination Dates</th>
<th>Post-Vaccine OPRA</th>
<th>Post-Vaccine Sera Ab Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/17/1987</td>
<td>0</td>
<td>Pfizer 0</td>
<td>2/12/21, 3/14/21</td>
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<td>6/1/21, 5/20/21</td>
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<tr>
<td>6/14/1967</td>
<td>0</td>
<td>Moderna 0</td>
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<td>0</td>
<td>6/17/21, 6/17/21</td>
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<tr>
<td>6/8/2014</td>
<td>0</td>
<td>Moderna 0</td>
<td>5/26/21, 6/23/21</td>
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<td>7/19/21</td>
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<td>1/13/1962</td>
<td>0</td>
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<td>3/6/2021</td>
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<td>3/10/1993</td>
<td>0</td>
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<td>5/5/21, 5/23/21</td>
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<td>5/25/21</td>
</tr>
<tr>
<td>3/25/1969</td>
<td>0</td>
<td>Moderna 0</td>
<td>3/15/21, 4/13/21</td>
<td>0</td>
<td>7/8/21</td>
</tr>
<tr>
<td>7/13/1953</td>
<td>0</td>
<td>Moderna 0</td>
<td>5/26/21, 6/17/21</td>
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<td>5/25/21</td>
</tr>
<tr>
<td>1/25/2799</td>
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<td>0</td>
<td>12/10/2021</td>
</tr>
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<td>3/10/1955</td>
<td>0</td>
<td>Moderna 0</td>
<td>3/16/21, 4/17/21</td>
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<td>6/7/21, 6/11/21</td>
</tr>
<tr>
<td>9/20/1959</td>
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<td>Pfizer 0</td>
<td>3/13/21, 4/15/21</td>
<td>0</td>
<td>6/27/21, 9/12/21</td>
</tr>
</tbody>
</table>

210.16

**Antibody Response to Booster mRNA COVID-19 Vaccine After Standard Doses of Various Homologous and Heterologous Vaccines in Kidney Transplant Recipients**

Ahram Han, Sangil Min, Eun-Ah Jo, Hye young Woo, Ara Cho, Hajoong Lee, Yong Chul Kim, Hee Kyung Kang, Yo Han Ahn, Eun Young Song, Jongwon Ha.

1Department of Surgery, Seoul National University College of Medicine, Seoul, Korea; 2Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea; 3Department of Pediatrics, Seoul National University Children’s Hospital, Seoul, Korea; 4Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Korea.

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210.17

Bacterial and Viral Infections After Kidney Transplant Before and After the COVID-19 Pandemic

Angelica Perez-Gutierrez1, Braden Juengel1, Sambhavi Krishnamoorthy1, Piotr J Bachul1, Piotr Witkowski1, Rolf N Barth1, John Fung1, 1Surgery, University of Chicago, Chicago, IL, United States.

Background: Infectious complications are a major cause of mortality and morbidity after kidney transplantation. During the COVID-19 pandemic there were several changes in the management and behavior of patients after transplant. These included measures such as universal masking, social distancing and reinforcing hand hygiene. Our objective was to evaluate if these differences affected the incidence of infections after kidney transplant.

Methods: This is a retrospective cohort study of all kidney transplants performed in our institution from March 2017 to November 2020. We examined the incidence of wound infection, urinary tract infection (UTI), pneumonia, and gastrointestinal (GI) infections. Pediatric and multi-organ transplants were excluded. We used the Fisher test, Chi-squared test of independence and logistic regression models in the analysis. All tests were based on a level of significance of α=0.05.

Results: A total of 185 deceased donor kidney transplant patients were reviewed, 153 before and 54 after the beginning of the COVID-19 pandemic in the United States. The incidence of wound infection, pneumonia and GI infection were similar before and after COVID (Table 1). There was a significant increase in UTI after the COVID-19 pandemic, the main organisms isolated were Klebsiella pneumonia (50%) and E. coli (25%) (Table 2). Overall the presence of UTI and wound infection were significantly associated (OR 4.2, p = 0.06). Other clinical variables such as age, body mass index (BMI), kidney donor profile index (KDPI), estimated post-transplant survival score (EPTS), and the occurrence of delayed graft function were not associated with UTI. The incidence of viral infections (CMV, EBV and BK viremia) was similar before and after COVID. Infections due to COVID-19 itself were present with similar incidence: 12% in patients transplanted before and 14.8% in patients transplanted after the onset of the pandemic. Induction with Thymoglobulin or Basiliximab was not significantly different before and after COVID (Table 1). There was a significant increase in UTI after COVID-19, and the choice of induction was not associated with the rate of UTI.

Conclusions: While multiple changes in the management of patients and patient behavior are different before and after the onset of the COVID-19 pandemic, this analysis did not find significant change in the incidence of infections except for UTI in comparative cohorts of kidney transplant recipients. This study did not identify specific factors associated with the increase of UTI in our population. However, in response certain measures were implemented, such as reducing the time to ureteral stent removal and giving 24 hrs of prophylactic antibiotics at the time of stent removal.

211.1

Effectiveness of Everolimus on Steroid-resistant Rejection After Liver Transplantation

Yang Won Nah1, Kyu Een Nah2, Jung Il Park1, 1Department of Surgery, Ulsan University Hospital, Ulsan, Korea.

Introduction: This retrospective study was done to assess our experience of Everolimus rescue therapy for steroid resistant rejection after liver transplantation.

Materials and Methods: Among 218 patients who underwent liver transplantation at Ulsan University Hospital during the period between April 2007 and October 2020, 44 patients received Everolimus as one of the post-transplant immunosuppressants. The indications for Everolimus was for renal protection in 23, immunologic causes in 13 and others in 8. Among the 13 patients who received Everolimus to control their suspected immunologic events, 7 patients were confirmed to experience steroid-resistant rejection. The effectiveness of Everolimus to rescue the steroid resistant rejection in these 7 patients was evaluated by the biochemical response, that is normalization of AST and ALT. The time point after liver transplantation when AST/ALT elevation drew medical attention and the value of AST/ALT at the time, implementation of liver biopsy and the result especially expressed as rejection activity index, use of steroid pulse therapy (SPT), time elapsed from liver biopsy to SPT, SPT to use of Everolimus, use of Everolimus to normalization of AST and ALT, respectively were investigated.

Results: The time point after liver transplantation when AST/ALT elevation drew medical attention vary widely from 15 days to 46 months after the liver transplantation and the mean value of AST and ALT at the time was 145 IU/L and 254 IU/L, respectively. Liver biopsy was performed in all patients and mean rejection activity index was 4.6. Steroid pulse therapy (500 mg/day, fixed dose for 3 days consecutively) was given to all the patients, two times in one patient. Everolimus was given because AST/ALT levels were not stabilized from 3 days to 51 days (median, 8 days) after the end of SPT. The mean values of AST/ALT were 146/310 IU/L and were higher than the values before SPT. It took a mean of 127 days (range, 31 – 360 days) for AST stabilization and 175 days (range, 51 – 390 days) for ALT stabilization. All the 7 events of SRR were amenable to Everolimus rescue therapy at a median of 91 days when evaluated by AST and ALT normalization.

Conclusion: Steroid-resistant rejection after liver transplantation was amenable to Everolimus treatment. Everolimus was induced at a median of 8 days after steroid pulse therapy. It took a median of 91 days for AST and ALT normalization for Everolimus rescue therapy. For generalization of the results of this study, a randomized controlled study in a large cohort is needed.

Table 1. Patients characteristics and clinical data

<table>
<thead>
<tr>
<th></th>
<th>Before COVID</th>
<th>After COVID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>57.0 +/- 24.8</td>
<td>53.0 +/- 12</td>
</tr>
<tr>
<td>Male</td>
<td>62.0%</td>
<td>68.5%</td>
</tr>
<tr>
<td>African American</td>
<td>59.7%</td>
<td>74.0%</td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>28.3 +/- 6.2</td>
<td>27.9 +/- 5.2</td>
</tr>
<tr>
<td>Cause of kidney failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HTN</td>
<td>24.8%</td>
<td>24.0%</td>
</tr>
<tr>
<td>Diabetic</td>
<td>28.7%</td>
<td>20.37%</td>
</tr>
<tr>
<td>Pump</td>
<td>39.2%</td>
<td>70.0%</td>
</tr>
<tr>
<td>DCD donor</td>
<td>45.0%</td>
<td>52.0%</td>
</tr>
<tr>
<td>KDPI (mean)</td>
<td>57.0 +/- 24.8</td>
<td>52.1 +/- 23.0</td>
</tr>
<tr>
<td>Rejection</td>
<td>11.7%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Death</td>
<td>12.4%</td>
<td>9.2%</td>
</tr>
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</table>

Table 2. Percentage of infections in kidney transplant recipients before and after COVID-19

<table>
<thead>
<tr>
<th></th>
<th>Pre COVID</th>
<th>Post COVID</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Wound infection</td>
<td>9.8</td>
<td>9.2</td>
<td>ns</td>
</tr>
<tr>
<td>UTI</td>
<td>44.4</td>
<td>29.6</td>
<td>0.002</td>
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<tr>
<td>Klebsiella</td>
<td>38.8</td>
<td>25%</td>
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<tr>
<td>E. coli</td>
<td>5.8</td>
<td>3.7</td>
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<tr>
<td>Pneumonia</td>
<td>9.8</td>
<td>11.32</td>
<td>ns</td>
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<tr>
<td>C.Diff</td>
<td>66.6</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>36.6</td>
<td>54.71</td>
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</tbody>
</table>
211.2

Lack of Differences in Safety and Effectivity Among Three Induction Immunosuppression Protocols During the First-year Post-Liver Transplantation in Pediatric Patients. A Multicenter Study

Alejandro Costaguta1, Guillermo Costaguta2, Daniel D’Agostino3, Gabriel Gondolesi4, Maria Belén Pallitto2, Carolina Rumbo3, Oscar Bottasso4, Fernando Alvarez5.

Introduction: Immunosuppression practice varies among centers. Very few comparative studies are published to define the best approach on an evidence-based background. Pediatric patients are ideal to explore potential differences due to their lower rate of comorbidities, being also a more homogeneous population (850% suffering from Biliary Atresia).

Methods: A retrospective, observational study of all patients receiving first liver transplantation in the four participating centers during a 5-year period (01/01/2015 to 12/31/2019) was conducted. Based on the type of immunosuppression administered on the immediate posttransplant setting, patients were classified as Group A (Basiliximab + Steroids + Tacrolimus), B (same as A + Thymoglobulin), and C (Steroids + Tacrolimus). Those patients with other schemes were excluded. Main analyzed variables were incidence of acute/chronic rejection, CMV/EBV or other viral/bacterial infections and first-year patient and graft survivals. A sub-set analysis on Biliary Atresia patients was also carried out in order to assess a more homogeneous population.

Results: 97 patients from 4 centers were recruited (Group A n= 52, Group B n= 25, Group C n= 20). Proportion of living donors were similar among groups (p=0.93). There were no differences in frequency of rejection (p=0.12), active CMV (p=0.10) or EBV (p=0.12) replication or development of other viral or bacterial infections (p=0.96) among groups, as well for patient (p=0.12) or graft (p=0.30) survival. Considering the 48 patients with Biliary Atresia (Group A n=26, Group B n=16, Group C n=6), frequency of rejection (p=0.64), EBV replication (p=0.92), and other infections (p=0.30) were similar; only CMV replication was more frequent in group B if compared to Group C (p=0.04). First year patient (p=0.61) and graft survival (100% in all groups) were similar regardless of the immunosuppression protocol employed in this series, either in the whole group or in the more uniform sample of those with Biliary Atresia. Since our study has been retrospective, a multicenter prospective properly powered study would be required to validate this conclusion.

Conclusion: Results during the first-year post-liver transplantation are comparable regardless of the immunosuppression protocol employed in this series, either in the whole group or in the more uniform sample of those with Biliary Atresia.

211.3

Effect of Preoperative Adjuvant Therapy on the Efficacy of Hepatocellular Carcinoma With Portal Vein Tumor Thrombus After Liver Transplantation

Ao Ren1,2, Yi Ma2

1Department of hepatobiliary surgery, The First Affiliated Hospital of Chongqing Medical University, Chongqing, People’s Republic of China; 2Organ Transplant Center, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, People’s Republic of China.

Introduction: Hepatocellular carcinoma (HCC) had a high incidence of portal vein tumor thrombus (PVTT), and the occurrence of PVTT usually indicated a poor prognosis. In recent years, liver transplantation has been recommended as an alternative treatment for HCC with PVTT, however the efficacy is still controversial. Preoperative adjuvant therapy had a certain effect in hepatectomy for HCC with PVTT, but its role in liver transplantation has not been reported. Therefore, the purpose of this study is to explore the effect of preoperative adjuvant therapy on the efficacy of HCC with PVTT after liver transplantation.

Methods: The clinical data of 22 patients with hepatocellular carcinoma with portal vein tumor thrombus (HCC + PVTT) undergoing liver transplantation from one center from 2010 to 2017 were analyzed retrospectively. 22 patients with hepatocellular carcinoma without portal vein tumor thrombus (HCC) were matched according to their age, tumor size and tumor number. The overall survival(OS) rate and recurrence-free survival(RFS) rate were compared between the two groups. At the same time, the OS and RFS of 22 patients with HCC+PVTT undergoing liver transplantation with preoperative adjuvant therapy and without preoperative adjuvant therapy were compared. Univariate and multivariate Cox regression analysis were used to explore the independent risk factors of recurrence.

Results: The 1- and 3-year OS in HCC + PVTT group were 63.64% and 30.69%, respectively, which were significantly lower than HCC group (81.57% and 52.78%, P = 0.0391, respectively). The 1- and 3-year RFS in HCC + PVTT group were 51.71% and 40.22%, respectively, which were significantly lower than HCC group (74.46% and 68.73%, P = 0.0407). In HCC + PVTT group, the 1- and 3-year OS in preoperative adjuvant therapy group were 70% and 40%, respectively, higher than non preoperative adjuvant therapy group (58.33% and 16.67%, P = 0.179), and the 1- and 3-year RFS in preoperative adjuvant therapy group were 88.93% and 63.49%, respectively, which were significantly higher than non preoperative adjuvant therapy group (20.37% and 20.37%, P = 0.0336). Univariate and multivariate Cox regression analysis showed that preoperative adjuvant therapy was an independent factor affecting recurrence after liver transplantation in HCC + PVTT group (P = 0.010 and P = 0.023).

Conclusion: This study was the first to explore the effect of preoperative adjuvant therapy on the efficacy of hepatocellular carcinoma with portal vein tumor thrombus after liver transplantation. In this study, the prognosis of patients with HCC + PVTT was poor. Preoperative adjuvant therapy can improve the prognosis of HCC + PVTT patients after liver transplantation and reduce the risk of recurrence. This study had certain clinical significance for exploring the preoperative treatment and operation timing of HCC with PVTT for liver transplantation. However, due to the small sample size of this study, which still need to be further verified by multi center large sample size research.
211.4
Characterization and Utilization of HCV-positive Donors in Argentina
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Background & Aims: Increased utilization of hepatitis C virus (HCV)-positive organ donors has been endorsed as one of several ways to combat organ shortages. However, HCV-positive donors remain poorly characterized and utilization of HCV-positive donors is unclear. Thus, we aimed to evaluate the prevalence and utilization of HCV antibody (Ab) positive donors in Argentina.

Methods: We performed a cross-sectional study to analyze data from the National Coordinating Institute of Ablation and Implant (INCUCAI) in Argentina from January 2006 to December 2020. Demographic and allograft characteristics were evaluated, and utilization of HCV Ab-positive donors across Argentina was studied. We included data from all donors, including effective organ donors (those for whom transplantation was effectively done), non-effective organ donors, and tissue only donors that were discarded. Anti-HCV (ELISA), was performed on all donors during the procurement process. A stratified analysis according to the type of donor and HCV Ab was done.

Results: Overall, 16,140 deceased donors were denounced. Of these, 8627 (53.5%) were organ donors (7802 [90.4%] were effective) and 7513 (46.5%) were tissue donors. Demographic characteristics were age 42 ± 18 years and male/female ratio was 1.59/1. HCV Ab-positive was reported in 0.92% (n=149). The highest prevalence of HCV was found in the provinces of Río Negro and Jujuy (1.19%), followed by Cordoba (1.1%) and the City of Buenos Aires (1.3%). Prevalence ratio per period among HCV Ab-positive donors showed that the highest prevalence was observed in 2007 (1.3%) and the lowest prevalence was in 2020 (0.1%). Prevalence for HCV Ab-positive among type of donors was significantly higher in non-effective donors 5.81% (n=48/825), followed by tissue donors only 1.01% (n=76/7513 and lower in effective donors 0.52% (n=25/4802; P<0.0001). Organ donors with HCV Ab-positive serology had less acceptance rate than those with HCV Ab-negative (34% vs 90%; respectively, p<0.001). The solid organ transplant plants performed using HCV Ab-positive donors were 23 kidney, 5 liver and 1 heart transplant; of these, only 4 transplants were performed after the advent of the new direct-acting antivirals in 2016. Five-year recipient and graft survival rates for liver grafts, median survival was 1.2 (0-12) years; 2 patients required a 2nd liver transplant; 4 pts lost the K re-starting hemodialysis, and 1 required intestinal graft removal.

Conclusion: The prevalence of HCV Ab-positive donors in Argentina is low and declining. Therefore, expanding the donor pool using HCV Ab-positive donors is a limited strategy in our country.

211.5
Long-term Experience of Liver Transplant Combined With Other Organs: A Single Center Analysis
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Introduction: Until a few years ago, combined liver transplantation with other organs (SLT+O) was unusual and limited not only by the small number of patients with this indication, but also by the lack of trained transplant centers. The scarce number of manuscripts reporting indications, benefits and long-term outcomes of a SLT+O, motivates our study.

Patients and Methods: Between July 2009 and December 2021, 56 patients (pts) received a SLT+O in our center; 42 (75%) were primary and 14 (25%) were re-transplants. Pts were divided into 3 groups according to type of transplant (Tx): liver-kidney (LK), liver-intestine or multivisceral (LI-M), and liver-heart or liver-lung (LHL). A retrospective analysis was performed using clinical, immunological and Tx variables. Main endpoints were pts and allografts survival. Statistical analysis: Chi square, T test, Kaplan Meier and log rank test. SPSS v20.0.

Results: 33/42 (78.5%) primary SLT+O pts received a LK, 6 (14.3%) a LI-M, and 3 (7.2%) a LHL Tx. All but 2 were adults, mean age 54 ± 15 years, 69% male; median follow up after Tx was 1.3 (0-12) years. Regarding the 14 re-transplants SLT+O, 12 were LK (85.7%) and 2 LI-M (14.3%), mean age 36 ± 18 years, 71% male; mean follow up after Tx was 2 (0-12) years. Main indication for SLT+O (primary or re-transplants) are listed in table 1. Regarding primary SLT+O actuarial survival at 5 years was 75% for LK, 66% for LHL, and 22% for LI-M, while for re-transplant was 63% at 1 year and 50% at 5 years, log rank 0.034 (figure 1). No statistical difference was found on pt survival between primary vs re-transplant SLT+O. Regarding graft loss: for liver grafts, median survival was 1.2 (0-12) years; 2 patients required a 2nd liver transplant; 4 pts lost the K re-starting hemodialysis, and 1 required intestinal graft removal.

Conclusions: Combined transplantation is currently a feasible procedure as an indication of multi-organ failure. Over time, Tx programs face the challenge of offering these procedures increasingly. Current results and outcomes are comparable to single organ transplant under multidisciplinary multiorgan transplant institutes.

Table 1.

<table>
<thead>
<tr>
<th>Liver</th>
<th>MELD 27+ 8.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol Cirrhosis (89%)</td>
<td></td>
</tr>
<tr>
<td>NAFLD (14.3%)</td>
<td></td>
</tr>
<tr>
<td>PCD (2.4%)</td>
<td></td>
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<tr>
<td>HCC 5%</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>Acute kidney Injury (31.0%)</td>
</tr>
<tr>
<td></td>
<td>Polycystic kidney disease (27.7%)</td>
</tr>
<tr>
<td></td>
<td>Idiopathic kidney disease (12.3%)</td>
</tr>
<tr>
<td>Intestine or multivisceral</td>
<td>Short bowel syndrome + parental nutrition associated liver disease (36.5%)</td>
</tr>
<tr>
<td></td>
<td>Grade IV portomesenteric vein thrombosis (15.7%)</td>
</tr>
<tr>
<td></td>
<td>Gardner’s Syndrome + renal artery thrombosis (15.7%)</td>
</tr>
<tr>
<td>Heart or Lung</td>
<td>Dilated myocardiopathy + cirrhosis (36.7%)</td>
</tr>
<tr>
<td></td>
<td>Cytic fibrosis with pulmonary and hepatic involvement (31.5%)</td>
</tr>
<tr>
<td>Renal transplant SLT+O</td>
<td>Etiology for the need of the other organ</td>
</tr>
<tr>
<td>Kidney: Calcium inhibitors nephrotoxicity in patients that required renal retransplant for ductopenic rejection (9-64.3%) and acute renal injury in a patient with chronic kidney disease that required renal retransplant (1-7.1%)</td>
<td></td>
</tr>
<tr>
<td>Liver: HCV cirrhosis in patients that required renal retransplant for chronic rejection (2-14.3%) and PNAOD thrombosis in patients that required intestinal retransplant (2-14.3%)</td>
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</tbody>
</table>
Introduction: Enhanced recovery after surgery (ERAS) has been shown to facilitate discharge, decrease length of stay (LOS), improve outcomes and reduce costs. We used this concept to design a comprehensive fast-track pathway (OR-to-discharge) before starting our liver transplant activity and then applied this protocol prospectively to every single patient undergoing liver transplantation at our institution, monitoring the results periodically. We report our results after a decade of activity.

Method: Prospective cohort study of all the liver transplants performed since we started our program in 2012. Balanced general anesthesia, fluid restriction, thromboelastometry, inferior vena cava preservation and temporary portocaval shunt were strategies common to all cases. Our standard protocol for immunosuppression included steroids, tacrolimus (delayed in the setting of renal impairment, with basiliximab induction added) and mycophenolate mofetil. Tacrolimus dosing was adjusted using a Bayesian estimation methodology. Oral intake and ambulation were started very early. LOS data refers to patients who were discharged (either from ICU or from the hospital) after transplantation.

Results: A total of 359 liver transplants have been performed in 341 patients (269M/72F) over 114 months, mean age 57.3±9.5 years, raw MELD score 15.2±7.8 (MELD-Na 17.1±8.1). Predominant etiologies were alcohol (n = 203) and HCV (n = 105), with hepatocellular carcinoma present in 187 (52.1%). Twenty-six transplants were URGENT (7%) and 15 of them were performed for Fulminant Hepatic Failure. Eighteen patients underwent combined liver and kidney transplants. The median operating time was 307 min (range 167–546) with median cold ischemia time of 267 min (130–628). We transfused PRBCs in the OR in 51 cases (14.2%) at an average of 2.4 ± 1.2 units per case. Median ICU LOS was 12.7 h, and median post-transplant hospital LOS was 4 days (2–82) with 52 patients (16.3%) going home by the 2nd posttransplant day, 133 (41.6%) by the 3rd, and 190 (59.4%) by the 4th, which defines the LOS of our fast-track group (2–4 days). Overall thirty-day-readmission rate was 34.7%, and it was significantly lower (27.9% vs. 44.6% P = 0.002) in the fast-track group. Patient survival was 88% at 1 year and 79% at 5 years for the entire series.

Conclusion: Fast-Tracking of Liver Transplant patients is feasible and remains the standard of care for our entire liver transplant population.
**211.7**

Is Pulse Oximetry a Good Screening Test for Hepatopulmonary Syndrome in Liver Transplant Candidates?

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**Background:** Pulse oximetry with oxygen saturation (SpO2) ≤96% is recommended as a screening test to identify patients (pts) with severe hepatopulmonary syndrome (HPS) to be eligible for MELD exceptions. However, diagnosis of milder forms requires contrast-enhanced echocardiography (CE-TTE) and arterial blood gas (ABG).

**Goals:** 1) To investigate the prevalence of intrapulmonary vascular dilatations (IPVD) and HPS in pts with cirrhosis evaluated for liver transplantation (OLT) and 2) To compare the results of SpO2 with ABG measurements.

**Methods:** The study included 972 consecutive pts (2013-2021) who completed pre-OLT evaluation including CE-TTE, SpO2 and ABG. IPVD was defined as the appearance of microbubbles in the left heart within 3-5 cardiac cycles and HPS by an alveolar arterial O2 gradient ≥ 15 mm Hg or ≥ 20 if age > 64 and absence of pulmonary chronic diseases. HPS was considered as mild, moderate or severe according to PaO2 (>80, 60-80 and <60 respectively).

**Results:** The prevalence of IPVD was 15.4% (150/972) and of HPS 7.8% (76/972). Age of pts with HPS was 47±3 years (57% males) and MELD-Na 17±1. HCV, alcoholism and autoimmune hepatitis were the most frequent etiologies of cirrhosis (22% each). Among pts with HPS 59 (78%) were mild (PaO2 108 ±22), 13 (17%) moderate (73 ±4) and 4 severe (55.5±3). SpO2 was ≤96% in 26% (20/76), 15% in mild (9/59), 54% in moderate (8/13) and 100% in severe (4/4) HPS. Unexpectedly, of 20 pts with Spo2 ≤96% only 4 had PaO2 <60 mmHg.

**Conclusions:** Universal testing with CE-TTE followed by ABG in patients with cirrhosis evaluated for OLT resulted in a lower prevalence than reported of HPS, most likely due to the preponderance of mild clinical forms with normal SpO2. Using the recommended cut-off value of SpO2 ≤96% we found a poor correlation between pulse oximetry and ABG measurement.

**211.8**

Impact of Sarcopenia Using Anterior Thigh Skeletal Muscle Index on Clinical Outcomes in the Liver Transplant Recipient

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**Backgrounds:** Sarcopenia is defined as loss of skeletal muscle strength, mass, and function. It has been reported as a significant risk factor for outcomes after Liver transplantation (LT) as well as waitlist mortality in end-stage liver disease patients. Although there are various imaging modalities and measurement methods for diagnosing sarcopenia, the gold standard is not clear. The purpose of this study is to analyze the effect of sarcopenia on outcome in LT patients using previously known third lumbar (L3)-skeletal muscle index (SMI) cut-off values and newly calculated anterior thigh (AT)-SMI cut-off values.

**Method:** Three hundred forty-one patients who underwent living and deceased donor liver transplantation in our center from Jan 2018 to Dec 2020 were analyzed. L3-SMI and AT-SMI were obtained by measuring preoperative computed tomography scans with semiautomatic software. For L3-SMI, the cut-off values reported in other previous studies were applied (42 cm²/m² in males, 38 cm²/m² in females). For AT-SMI, the optimal cut-off value was obtained by the ROC curve for sarcopenia.

**Results:** The prevalence of sarcopenia diagnosed by L3-SMI was 29.9 % (102/341) and by AT-SMI was 35.5% (121/341) in our cohort. The cut-off values of AT-SMI obtained by ROC curve were 12.6 cm²/m² for female (AUC = 0.915, P < 0.001) and 14.2 cm²/m² for male (AUC = 0.882, P < 0.001). Patient and graft survival rates in the sarcopenia group by AT-SMI were significantly lower than in the non-sarcopenia group (P < 0.001, P < 0.001). AT-SMI was identified as one of the independent prognostic factors in patient survival in multivariable cox analysis, whereas L3-SMI was not (HR, 4.462; 95 % CI, 1.792 – 11.106; P = 0.001). It was also confirmed by ROC curve analysis that AT-SMI was more highly correlated than L3-SMI for patient survival (P = 0.005).

**Conclusion:** Both the L3-SMI and AT-SMI-induced sarcopenia group had a significantly lower patient and graft survival than the group without sarcopenia. However, AT-SMI was identified as an independent prognostic factor for patient survival and was more correlated with patient survival than L3-SMI. This means that AT-SMI may be a better option than L3-SMI for the evaluation of CT-based sarcopenia in LT recipients.
Liver Function for Over 100 Years in 2 Different Individuals - the Centennial Liver Allograft has Arrived

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Background: Previously we studied the occurrence of deceased-donor liver (DDLT), deceased-donor renal (DDRT), and living-donor renal allografts (LDRT) that have achieved or come close to 100 years of function in 2 different individuals. We reported that extended longevity is higher among liver vs. kidney allograft recipients.

Purpose: We investigated the incidence, demographics and function of DDLT allografts that have achieved or come close to 100 years of physiologic function in 2 different individuals.

Methods: Liver allograft survival was calculated according to the equation: Liver allograft survival = Liver allograft age at donation + Liver allograft survival. The following age groups were studied: (1) 90-94 years, (2) 95-99 years, or (3) 100 years and longer. Graft survival was defined as function time to date, most recent follow-up or death, re-listing for transplant. Multivariate analysis assessed predictors of physiologic allograft survival > 90 years. In total, there were 502 deceased donor liver allografts > 90 years of age reported to UNOS/OPTN from 10/87 to 05/21; There are no DDLT with >90 year of allograft function.

Results: Table 1 shows the characteristics and outcomes. Outcome of DDLT increased over time in general and 502 grafts showed physiological function > 90 years. In 19 cases, the duration of function was > 100 years; the longest graft function time was 108.3 years. Of the 19 recipients, 10 still have a functioning allograft (longest survival: 106.9 years and counting in a 69-year old recipient who received a 92-year old donor liver); donor age was >90 years in 5 donors; >80-89, in 12; >70-79 in 2. Of allografts with >95 years, donor age was >90 in 5 and >80-89 in 51 cases. Multivariate analysis of each cohort verified that good donor and recipient management factors are potential predictors of allograft longevity.

Conclusion: (1) Organ longevity in 2 different individuals exceeding 100 physiologic years is possible: We identified 19 liver recipients with >100 years in liver function and 502 recipients >90 years. This represents a small but increasing minority of grafts in liver transplant recipients. It is expected that more grafts will reach this mark with increasing follow-up time. (2) Over half of grafts in liver transplant recipients. It is expected that more grafts will reach this mark with increasing follow-up time. (3) Over half of the allograft function in 2 different individuals.

Evaluating the Impact of Kidney Transplant Timing on Postoperative Dialysis Requirement and Mortality in Liver Transplant Patients: A Single Center Experience

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Purpose: Renal insufficiency often occurs in patients with cirrhosis awaiting liver transplantation (LT). Although some of these patients require kidney transplantation (KT), guidelines on allocating kidney grafts for LT candidates continue to evolve. The aim of this study was to evaluate the outcomes of combined liver-kidney transplantation, compared with LT alone, and develop a new risk index for dialysis requirement at 12-month-post-LT (12M-pLT).

Methods: Adult LT recipients at our institution between January 2017 and December 2020 were retrospectively reviewed. Patients receiving LT for malignant tumors were excluded. LT patients were divided into two groups, simultaneous liver-kidney transplant (SLKT) and no SLKT. The no SLKT group was further divided into LT alone (LTA) and KT after LT (L-K). Dialysis requirement at 12M-pLT was assessed across all groups. Survival and multivariate analyses were performed to identify risk factors for dialysis at 12M-pLT.

Results: 541 out of 598 patients were included. The physiologic median model for end-stage liver disease (MELD) score was 35. 507 (87%) were on dialysis at time of SLKT or LT. 59 (11%) received SLKT and 31 (6%) eventually received a kidney graft after LT (L-K). Among the SLKT, LTA, and L-K groups, L-K showed a tendency for higher survival rates at 3-year-post-LT (SLKT: 74%, LTA: 83%, L-K: 100%); however, there was no significant difference after 3 years. SLKT and LTA patients on dialysis at 12M-pLT had significantly lower survival than those not on dialysis (p=0.008 in SLKT, p<0.001 in LTA). Only 32% of LTA patients remaining on dialysis at 12M-pLT ultimately recovered from it (Figure 1A). SLKT had the highest and earliest withdrawal rate from dialysis at 12M-pLT of 96% (LTA: 82%, L-K: 26%, p<0.001). In L-K patients, median wait time for KT was 15 months; ultimately, these patients reached a 100% withdrawal rate post-KT (Figure 1B). Multivariate analysis of no SLKT patients identified dialysis at LT (OR 11.115, <0.001), pre-LT mechanical ventilation (OR 1.854, p=0.029), and coronary artery disease (OR 1.871, p=0.04) as independent risk factors for dialysis at 12M-pLT. Based on the OR, we assigned a score for each risk factor and developed a new index (c-statistic 0.796). This index significantly correlated with increased incidence of dialysis 12M-pLT (3% in score 0, 55% in score 5–6, p<0.001).

Conclusion: This analysis examined LT outcomes and dialysis independence with or without KT in the era of the kidney rescue pathway. SLKT had the highest withdrawal rate from dialysis postoperatively. Post-LT dialysis at 12M had lower survival. Independent risk factors for post-LT dialysis at 12M-pLT may serve to guide perioperative management, and kidney graft allocation in high acuity LT recipients.
Successful Reversal of Propionic Acidemia Associated Cardiomyopathy After Pediatric Living Donor Liver Transplantation: A Case-based Review

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Introduction: Propionic acidemia (PA) is a rare mitochondrial metabolic disorder involving multiple organs throughout the body. Since adherence to recommended conservative metabolic management cannot reliably prevent disease progression, liver transplantation (LT) is emerging as a viable alternative therapeutic option in selected PA patients. However, therapeutic outcomes of LT for PA-associated cardiomyopathy are rarely reported.

Method: A thorough review of the current published literature was performed to evaluate outcomes of LT for patients with PA-related cardiomyopathy. Clinical, biochemical, and neurophysiological outcomes were compared with the 2-year-old female child managed at our institution.

Results: The pretransplant echocardiogram showed left ventricular dilatation and systolic dysfunction, and thus dilated cardiomyopathy was considered. A living donor liver transplant was performed using the mother’s left lateral lobe. On the 35.8 months postoperatively, the child was on a liberated protein diet, but still required levocarnitine supplementation. The hepatic and cardiac function were both normal, but growth retardation was still present. During the follow-up period, there were no further propionic acidemia-related complications, such as metabolic decompensation, or any transplant-related complications. Published literature revealed that the cardioprotective potential of LT for individuals with PA has been proved by the fact that reversal of cardiomyopathy was achieved in all previously reported 11 pediatric patients with pre-existing PA-associated cardiomyopathy. In line with previous results, our patient with mild dilated cardiomyopathy also displayed a complete recovery of cardiac function after LT.

Conclusion: This case report and systematic review demonstrates that LT can successfully treat patients with PA-related cardiomyopathy, which relieves strict protein restriction, provides systemic metabolic stability, improves quality of life, and reverses cardiomyopathy. Nevertheless, recipients with PA remain at risk of developing PA-related complications including cardiomyopathy.
No Difference in Posttransplant Survival Among Patients With or Without Nonalcoholic Steatohepatitis: A Meta-analysis and Meta-regression

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Background & Aims: Nonalcoholic steatohepatitis (NASH) is a dramatically growing indication for liver transplantation (LT) worldwide. The posttransplant outcomes of NASH patients are currently under intensive investigation. Given the enormous volume of new studies with inconsistent results, we conducted a meta-analysis aimed to update the clinical evidence on the long-term outcomes of transplanted patients with NASH.

Methods: We comprehensively searched MEDLINE, Embase, Cochrane Library, and Web of Science databases through September 15, 2021, for comparative studies focusing on outcomes of LT recipients with NASH and indications other than NASH. Random-effects meta-analysis was conducted to calculate pooled odds ratios (ORs) and 95% confidence intervals (CIs). Meta-regression was used to examine hepatocellular carcinoma (HCC) as a confounder on patient survival.

Results: Twenty-two studies with 1,538 NASH and 6,014 non-NASH patients were included. 1- (OR, 0.94; 95% CI, 0.77–1.14), 3- (OR, 0.82; 95% CI, 1.00–1.22), and 5- (OR, 1.05; 95% CI, 0.84–1.31) year patient survival was equivalent between NASH and non-NASH recipients. NASH patients were associated with similar cardiovascular mortality (OR, 1.36; 95% CI, 0.89–2.09) and retransplantation rates (OR, 0.69; 95% CI, 1.03–1.53), lower graft failure-related mortality (OR, 0.11; 95% CI, 0.29–0.74), but higher sepsis-related mortality (OR, 1.53; 95% CI, 1.13–2.06). In meta-regression analysis, the proportion with HCC showed a strong correlation with posttransplant survival.

Conclusions: This pooled analysis of a large global sample size showed no difference in posttransplant survival between NASH and non-NASH patients. NASH recipients should be managed with caution after LT, especially regarding the potentially high risk of sepsis-related death.
Five Cases of Familial Hypercholesterolemia Treated by Liver Transplantation

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Objective: To investigate the clinical effect and prognosis of liver transplantation for familial hypercholesterolemia (FH).

Method: A retrospective analysis was performed on the preoperative characteristics, operative conditions and postoperative follow-up of 5 children who received liver transplantation for familial hypercholesterolemia admitted to our center from December 2014 to July 2021.

Result: The patients’ primary clinical manifestation was a progressive increase of palpable yellow masses in buttocks and joints and decreased activity tolerance, accompanied by increased blood cholesterol and low-density lipoprotein. Case 1 had multiple coronary artery stenosis and intra-arterial lipid plaque formation. Case 2 had severe stenosis of the coeliac trunk, multiple stenoses of neck vessels, and repeated chest tightness and precordial pain after exercise. Case 3 had carotid intima-media thickening and right subclavian artery plaque formation. Case 4 showed uneven thickening of intima-media membranes of bilateral external iliac arteries and bilateral carotid arteries. Case 5 showed slight thickening of intima-media membrane at the beginning of bilateral carotid arteries and right subclavian artery, and slight stenosis of descending aorta. All patients were confirmed to have FH by genetic test and biochemical blood test. Case 2 gene test was compound heterozygous LDLR mutation (exon6; c.920A>G); case 3 gene test was compound heterozygous LDLR mutation (exon4; c.G665T; exon14; c.C2054T); case 4 was homozygous LDLR mutation (exon7; c.G952T>C); case 5 was a composite heterozygous LDLR mutation (exon5; c.727T>A; exon9; c.1187-10G>A). The age of the first onset were 6 years, 4 years, 2 years, 4 years, 2 years, 1 year, and 1 year, respectively. All 5 children were male, with the preoperative blood cholesterol level of 15.33±4.67mmol/L and the blood LDL level of 10.69±2.80mmol/L. Preoperative low-fat diet and lipid-lowering drugs, including rosuvastatin, ezetimibe, probucco and Xuzhikang, had poor efficacy. They received liver transplantation at 149, 124, 92, 45 and 72 months, and all donor livers were from cadavers. On the first day after liver transplantation, their blood cholesterol level was 5.56±1.88mmol/L and their LDL level was 4.06±1.75mmol/L. Preoperative low-fat diet and lipid-lowering drugs, including rosuvastatin, ezetimibe, probucco and Xuzhikang, had poor efficacy. They received liver transplantation at 149, 124, 92, 45 and 72 months, and all donor livers were from cadavers. On the first day after liver transplantation, their blood cholesterol level was 5.56±1.88mmol/L and their LDL level was 4.06±1.75mmol/L. All the children have survived healthy. The cardiocerebrovascular diseases of the 5 children have not shown significant progress in postoperative follow-up so far. The clinical manifestations such as suffocating, squatting and precordial discomfort were significantly reduced in postoperative follow-up so far. The clinical manifestations such as suffocating, squatting and precordial discomfort were significantly reduced in postoperative follow-up so far.

Outcome: All the children survived and were healthy. The blood cholesterol level was in the normal range and normal diet was resumed. The patients have been followed up for 80.7, 24.1, 11.3, 9.6 and 6 months. All the children have survived healthy. The cardiovascular diseases of the 5 children have not shown significant progress in postoperative follow-up so far. The clinical manifestations such as suffocating, squatting and precordial discomfort were significantly reduced after operation.

Conclusion: Liver transplantation is a means to cure FH. It should be performed before the occurrence of cardiovascular diseases in children, and satisfactory quality of life can be achieved after transplantation.
Effect on Kidney Transplant Allocation With the Implementation of Concentric Circles Liver Allocation Policy: Impact of Simultaneous Liver Kidney Transplantation

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Introduction: Although the new acuity circle allocation (ACA) policy has had an improvement in liver transplant (LT) rates in the United States, its effect on other solid organ transplants is unknown. The ACA has likely resulted in institutional and regional changes in the distribution of deceased donor kidneys as well, especially in the setting of simultaneous liver kidney (SLK) transplantation. We sought to review SLK patterns before and after the institution of ACA and determine if SLK rate changes were associated with a change in kidney transplant (KT) rates and patient and graft survival.

Methods: Data from the Scientific Registry of Transplant Recipients (SRTR) was analyzed to evaluate rates of SLK transplantation before and after the implementation of ACA. Era 1 was defined as January 1, 2018 to February 3, 2020; Era 2 was defined as February 4, 2020 to June 1, 2021. Statistical comparisons between eras were performed. Transplant programs were divided into high (25%ile), medium (26-74%ile), and low volume (75%ile) KT programs according to Era 1. Similarly, transplant programs were divided into high (25%ile), medium (26-74%ile), and low volume (75%ile) SLK programs according to Era 1. Transplant volume was assessed for Era 2.

Results: We analyzed 28,085 SLK and 75,058 KT performed in adult recipients from January 1, 2018 to June 1, 2021; 16,799 SLK and 45,168 KT were performed in Era 1 and 11,286 SLK and 29,890 KT were performed in Era 2. For SLK recipients during Era 1, the 1- and 3-year patient survival was 90.3% and 75.9%, respectively; the 1- and 3-year graft survival was 97.4% and 96.8%, respectively. During Era 2, the 1-year patient and graft survival for SLK recipients was 85.8% and 97.5%, respectively. For KT recipients during Era 1, the 1- and 3-year patient survival was 97.1% and 87.6%, respectively; graft survival was 97.5% and 93.1%, respectively. During Era 2, the 1-year patient and graft survival for KT recipients was 92.6% and 96.9%, respectively. As a result of ACA, 1,008 additional kidneys went to SLK recipients while both patient and graft survival decreased for KT as a result of ACA.

The Role of Liver Transplant in the Management of Hepatoblastoma Patients

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Background: Hepatoblastoma (HB) is a rare malignancy. Liver resection (LR) and liver transplant (LT) are potential curative treatment, but the selection strategy for LT remains unclear. This study aimed to define the selection criteria between LR and LT. Method This was a retrospective study from 2 university centers. All patients with HB who received chemotherapy and surgical treatment from 2014 to 2020 were included. Patients who had unresectable disease after chemotherapy would be offered LT. Salvage LT would be considered if patients developed recurrence after LR. Multivariable analysis was conducted to identify risk factors for inferior event free survival (EFS) after LR and to determine the impact of such risk factors in the LT cohort.

Results: One hundred and fifty-one HB patients were included; 133 (88.1%) patients had primary LR and 18 (11.9%) had primary LT. The flow chart of all study patients was presented in Figure 1. As LT was reserved for patients who had unresectable disease after chemotherapy, the POST-LR stage was more advanced in the primary LT group. (Table 1) Nonetheless, the overall survival (OS) and EFS were similar between primary LR and primary LT group. Figure 2a and 2b. In multivariable analysis among the LR group, 2 risk factors were associated with poor EFS: multifocality HR 3.294 95% CI (1.739-6.243), P <0.001 and rupture HR 3.772 95% CI (1.321-10.777), P=0.013. The LT group were stratified into 2 groups based on the presence of risk factors. The 5-year EFS after LT was 87.1% and 80.2%, in the absence and presence of risk factor respectively. (Figure 3) Fifteen patients underwent salvage LT and their outcomes were compared to patients who underwent primary LT. The OS and EFS were comparable. (Figure 4a and 4b).

Conclusion: HB patients who had multifocal disease and rupture were associated with inferior EFS and LT should be considered. The outcomes of salvage LT were comparable to primary LT and it should be offered as a curative treatment in patients with recurrent HB.
Normothermic Machine Perfusion and Orthotopic Allotransplantation of the Full Length Porcine Intestine

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Background: A limitation of intestinal transplantation is severe graft injury during cold storage, leading to sepsis and rejection. Improved graft preservation will improve post-transplant outcomes. Recently, trials of oxygenated machine perfusion (MP) in liver transplantation show superior outcomes compared to cold storage. We hypothesized oxygenated MP of intestinal grafts would be feasible and improve outcomes after intestine transplantation, similar to other transplanted organs. The aim of this study was to develop a translational normothermic machine perfusion (NMP) protocol of full-length intestine allograft and validate feasibility of MP by orthotopic transplantation in a porcine model.

Methods: The NMP protocol underwent 3 iterative stages of development, generation 1, 2, and 3 (GEN1, GEN2, GEN3). GEN1 (n=8 grafts) protocol was adapted from published liver NMP protocols. Changes were made after review of 6-8 graft perfusions with a standardized approach. The perfusion circuit consisted of a graft chamber with open venous return into a reservoir below. A roller pump circulated perfusate from the reservoir into the oxygenator into the craniomesenteric artery at a mean arterial pressure of 50 ± 5 mmHg for 6 hours. Vasodilators were administered into the arterial line by constant infusion. Perfusion pressure, temperature, and arterial flow were monitored continuously using in-line sensors. A dialysis circuit was used to maintain the normal chemistries in GEN2 & 3. We compared gross and histologic appearance of paired samples from the time of organ procurement and after six hours of oxygenated MP. After optimization, transplantation of porcine intestine allografts after 6 hr NMP were then undertaken and post-operative recovery of gut function, physical activity, oral intake and maintenance of normal vital signs and lab values were monitored for 2 days before sacrifice.

Results: During protocol development, we identified several factors that appear unique to the intestine allograft and posed challenges during MP, including metabolic, electrolyte, acid-base disturbances, as well as differential perfusion of the jejunum and ileum. These factors coincided with graft and mesenteric edema, luminal hemorrhage, and ileal ischemia with the initial protocol. Addition of dialysis and introduction of vasodilating medications corrected the metabolic derangements in perfusate chemistries, and gross and histologic appearance suggested excellent preservation in GEN3. We report successful transplantation of 3 porcine intestinal allografts after MP with excellent post-operative recovery of gut function, physical activity, oral intake and maintenance of normal vital signs and lab values. At 48 hours inspection of the bowel graft demonstrated viable pink serosa without evidence of mucosal injury.

Conclusions: This study reports development and optimization of machine perfusion preservation of small intestine and successful transplantation of the intestinal allograft in a porcine model.

U.S Department of Defense (DOD).
Eliminating Second Warm Ischemia in Order to Address the Organ Shortage, Increase Transplant Longevity, and Enable Minimally Invasive Kidney Transplantation: Ex-vivo Validation of a Kidney Anastomosis Facilitation and Cooling Device Developed Via the Biodesign Process

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¹Department of Surgery, UCSF, San Francisco, CA, United States; ²Division of Transplantation, UCSF, San Francisco, CA, United States.

Introduction: Kidneys are particularly susceptible to anoxic damage and ischemia due to their aerobic metabolism. Hypothermia protects against anoxia by reducing the energy dependent metabolic activities and is optimally achieved at 1-2°C for cold storage and 4-8°C for machine perfusion during transportation. There are no effective methods to prevent warming during implantation. The warming of a donor kidney during the vascular anastomosis of a transplant i.e., second warm-ischemia time (SWIT), is independently associated with higher rates of delayed graft function, premature graft failure, and the discard of high-risk kidneys. SWIT is protracted in patients with complex anatomy, obesity, and in minimally invasive transplantation. Elimination of SWIT via intra-operative thermal regulation has the potential to increase the donor pool and proffer significant cost-savings.

Method: The objective biodesign process was used to identify this clinical need through observation, develop a needs statement, and filter the need against others. A needs-specification document was developed outlining stakeholder value propositions, health-economic value, and existing intellectual property. ASTS surgeons (n=185) and organ-preservation specialists were surveyed to develop the needs-criteria for a device. The invention step resulted in several embodiments that addressed the clinical need, population, and outcome outlined in our needs statement. Following objective concept selection, a prototype device applied to the kidney immediately prior to anastomosis was built using stretchable hydrogel and phase-change gel. Adult porcine kidneys were used to test the device in a validated retroperitoneal-model placed within a water bath at 37°C (98.6°F). Core temperatures were monitored using implanted probes at 30 second intervals. Time to reach the maximum ischemic threshold of necrosis (15°C, 59°F) was compared to an ice + gauze control.

Results: A single-use device to facilitate the vascular anastomosis and eliminate SWIT was developed. The needs-criteria were addressed with a retraction handle, no tubing, a low profile, and a flexible material to accommodate variable kidney sizes. The device-covered kidneys (n=3) did not reach the ischemic threshold at the 60-minute cutoff and remained below 6°C compared with the ice + gauze covered control kidneys (17±1.8 minutes, n=3, p <0.001).

Conclusion: A breakthrough designated medical device to facilitate the vascular anastomosis and effectively eliminate second-warm-ischemia time was successfully developed. Device-covered kidneys remained well below the ischemic threshold of necrosis for a duration exceeding 95% of vascular anastomoses. Use of this device will enhance the surgical workflow and enable minimally-invasive transplantation and has the potential to significantly impact rates of delayed graft function, organ longevity, and organ acceptance practices.
PERLA, a New Cold-storage Solution to Preserve Liver Grafts From Extended Criteria Donors

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Background: The composition of cold storage solutions is a critical factor to maintain the quality of the transplanted grafts. The University of Wisconsin (UW) preservation solution is the most used in liver transplantation. However, it shows important limitations, especially when grafts are derived from extended criteria donors, such as steatotic livers or they are submitted to prolonged ischemic periods. The UW solution contains HES (inducing erythrocyte aggregation), high-K+ concentration (causing hyperkalemic cardiac arrest) and some drugs like allopurinol, GSH or adenosine which do not confer any protection. We have developed a new liquid called PERLA® (patented by Barcelona University; PCT/ES2009/000267). It is a high-Na+ liquid containing polyethylene glycol-35, carbediol, trimetazidine and tacrolimus. These three last molecules are potent modulators of the main pathways responsible of ischemia-reperfusion (IR) injury. We evaluated the effectiveness of PERLA® compared to UW solution in preserving non-steatotic and steatotic rat livers.

Methods: Two models were used: the isolated perfused liver and the orthotopic liver transplantation. Homozygous (obese) and heterozygous (lean) Zucker rats between 16 and 18 weeks were used. In the ex vivo perfused model, grafts were cold preserved for 24h using either UW or PERLA® solution and then, they were perfused ex vivo for 120 min at 37°C. In vivo model, steatotic and non-steatotic grafts were cold stored for 6h using either UW or PERLA® solutions and transplanted to rats. Hepatic functionality and damage were measured by quantifying transaminases (ALT/AST), bile flow and the morphological changes of liver were observed by HE staining. The protein expressions of PPARγ, NRF2, KEAP1, NQO1 and HO-1 were detected by Western bolting, and the mRNA levels of TLR-4, TRIF and MYD88 were measured by qPCR. The postoperative survival rate was evaluated.

Results: Serum ALT and AST levels in HOPE group were 4094±778.156 U/L and 6869.6±1324.486 U/L, respectively, 6 hours after liver transplantation. Serum ALT and AST in Rosiglitazone group were 3783.2±851.737 U/L and 4773.6±1105.611 U/L, respectively, without statistical significance (P >0.05), while the expression of MYD88 did not change significantly, suggesting that the enhanced anti-immune response of HOPE may be related to the activation of PPARγ by TBP and the inhibition of TRIF-4/TRIF pathway. Compared with the 1-week survival rate, the survival rate of the normal liver group was 100% (6/6), the survival rate of the CS and HOPE groups were 50% (3/6) and 83% (5/6), respectively. The main causes of death within 24 hours were pulmonary embolism and postoperative hypothermia, and the main cause of death within 7 days was biliary complications.

Conclusion: HOPE enhanced the activity of PPARγ and the repair mechanism may be related to NRF2/PPARγ and TRIF-4/TRIF signals, providing a new trail for DCD donor-derived liver. Key words: liver transplantation; hypothermic oxygenated machine perfusion; donation after cardiac death; tetramethylpyrazine: PPARγ; NRF2.

Tetramethylpyrazine Alleviates Liver Ischemia-reperfusion Injury of Transplantation in Rat Model From Donation After Cardiac Death via Activation of PPARγ/Nrf2 Signaling Pathway

Fu Zheng1, Fan Lin1, Ye Qi Fa1,2

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Background: 45% of Liver grafts from donation after cardiac death (DCD) are discarded for transplantation because of their poor tolerance to ischemia reperfusion injury (IRI). Based on the previous research, tetramethylpyrazine(TMP) could reduce liver IRI of DCD in rats model, but the molecular mechanisms are unclear.

Objective: This work aims to investigate the molecular mechanisms, it would provide effective ideas for protective effect of TMP on improving the quality of DCD donor-derived liver transplantation, and its repair mechanism may be related to NRF2/PPARγ and TRIF-4/TRIF signals, providing a new trail for DCD donor-derived liver. Key words: liver transplantation; hypothermic oxygenated machine perfusion; donation after cardiac death; tetramethylpyrazine: PPARγ; NRF2.

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Donor in Situ Ischemia Time (DISIT) in Kidney Transplantation

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Introduction: Multiple factors in organ retrieval and transplantation influence the short-and long-term renal allograft outcome. Donor In Situ Ischaemia Time (DISIT) is the time from commencement of cold perfusion in the deceased donor, until the organ is removed and placed within ice. We studied the association between DISIT and short time graft function in kidney transplant recipients.

Methods: Using data from 540 consecutive kidney transplants between 1st of January 2014 and 1st of January 2022, we assessed the association between DISIT and graft function post-transplant using a multivariable ordinal logistic regression, adjusted for DCD status, donor sex and age, and KDPI. We defined graft function as immediate, slow graft and delayed graft function. In a subset of our cohort, n = 47, histological assessment (cv score – Banff criteria for chronic vasculitis) of the allograft was assessed using a linear regression.

Results: The mean age (SD) of the transplant recipient was 51.69 (12.89), with median DISIT time of 34 minutes. For every one-minute increase in the DISIT, odds of developing slow graft function and delayed graft function versus immediate graft function is 3.3 times higher, given all other variables are held constant. the DISIT correlated significantly with initial renal allograft function (p<0.05). Further, DISIT was also correlated with an increase in cv score during the first 12-months post-transplantation (p<0.01).

Conclusion: These results demonstrate the importance of minimising this novel ischaemia time as a way of reducing the incidence of short- and long-term graft injury.

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Heart Transplantation Using Donation After Circulatory Death Donors – an 8 Year Experience

Claudio Soto1, Yashutosh Joshi1, Sarah Scheuer1, Hong Chew1, Arjun Iyer1, Andrew Dinale1, Paul Jansz1, Peter MacDonald1.
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Donation after circulatory death (DCD) is a technique utilising the heart from donors after withdrawal of life support and requires the donor to sustain circulatory cessation prior to organ retrieval. Our unit was the first to perform heart transplants utilising distantly procured hearts from DCD donors in 2014. We report the experience at our institution and lessons learnt throughout this period.

Methods: Using data from 540 consecutive kidney transplants between 1st of January 2014 and 1st of January 2022, we assessed the association between DISIT and graft function post-transplant using a multivariable ordinal logistic regression, adjusted for DCD status, donor sex and age, and KDPI. We defined graft function as immediate, slow graft and delayed graft function. In a subset of our cohort, n = 47, histological assessment (cv score – Banff criteria for chronic vasculitis) of the allograft was assessed using a linear regression.

Results: The mean age (SD) of the transplant recipient was 51.69 (12.89), with median DISIT time of 34 minutes. For every one-minute increase in the DISIT, odds of developing slow graft function and delayed graft function versus immediate graft function is 3.3 times higher, given all other variables are held constant. the DISIT correlated significantly with initial renal allograft function (p<0.05). Further, DISIT was also correlated with an increase in cv score during the first 12-months post-transplantation (p<0.01).

Conclusion: These results demonstrate the importance of minimising this novel ischaemia time as a way of reducing the incidence of short- and long-term graft injury.

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Ngee-Soon Lau1,2,3, Mark Ly1,2,3, Claude Dennis5, Joanna Lou Huang1,2,3, Joanne Huang1,2,3, Andrew Jacques1,2,3, Marti Cabanes-Creus2,4, Shamus Toomath1,2, Nicole Mestrovic1,2,3, Paul Yousif1,2, Sumon Chanda1,2, Chuanmin Wang1,2,3, Leszek Lisowski4, Ken Liu1,3, James Kench3,5, Geoffrey McCaughan1,2, Michael Crawford1,2, Carlo Pulitano1,2,3.
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Introduction: Current ex-vivo technology allows the perfusion of an organ only for a number of hours. There is a need for perfusion in the range of days-to-weeks to facilitate sophisticated assessment, recovery and modification of these organs. Normothermic perfusion of livers longer than 1 week has never been previously described. In this study, we aimed to develop a model which reliably maintained the physiological function of human livers for more than 1 week and understand the requirements of these organs for long-term survival.

Method: We developed a protocol for long-term organ perfusion using a modified commercial system which included long-term oxygenators, a gas-mixer and a dialysis filter. Human livers not suitable for transplantation were perfused using a human red-cell based perfusate under normothermic conditions (36°C) and then surgically split without interruption to perfusion. The resulting left lateral segment grafts and extended right grafts were then perfused on separate machines for the purpose of long-term survival and individual graft assessment with biochemical and histological markers of liver function (Figure 1). Novel methods for understanding the cause of graft failure of these human livers in the long-term were used including indocyanine green perfusion, microbial cultures, lipidomics, metabolomics and assessment of pro-inflammatory cytokines.

Results: Ten livers underwent a conventional split during normothermic perfusion resulting in 20 partial grafts. The median ex-vivo survival was 165 hours, and the longest survival was 328 hours (13 days) (Figure 2). Graft survival was demonstrated by lactate clearance, bile production and production of Factor-V in the long-term. A total of 9/20 (45%) grafts survived for ≥7 days. These grafts demonstrated a significantly higher bile production adjusted to graft weight and a significantly higher level of perfusate Factor-V in the first 48 hours of perfusion (Figure 2). All grafts eventually failed with a predictable and repeatable pattern which include: increasing vascular resistance, unresponsive hypoglycaemia, acidosis and growth of mixed flora microbial contaminants.

Conclusion: We report a reliable and repeatable protocol for the long-term ex-vivo perfusion of human livers for more than 1 week. Possible reasons for organ failure during long-term perfusion include overwhelming infection and a failure to meet all long-term metabolic requirements. Future work should aim to overcome these barriers with the goal of preservation for weeks-to-months, if not indefinitely.
Brief Bubble, and Subsequent Intermittent Surface Oxygenation Is a Simple and Effective Alternative for Membrane Oxygenation to Maintain Aerobic Metabolism During Hypothermic Machine Perfusion in Kidneys

Tom Darius1,2, Martial Vergauwen2, Louis Maistriaux2,3, Robin Evarard4, Matteo Mueller2, Philipp Dutkowski5, Andrea Schlegel5, Philipp Dutkowski5, Pierre Gianello2, Michel Mourad1,2.
1Department of Surgery, Surgery and Abdominal Transplant Unit, University Clinics Saint-Luc, Université catholique de Louvain, Brussels, Belgium; 2Institut de recherche expérimentale et clinique (IREC), Pôle de Chirurgie Exp et Transplantation, Université catholique de Louvain, Brussels, Belgium; 3Institut de recherche expérimentale et clinique (IREC), Pôle de Morphologie, Université catholique de Louvain, Brussels, Belgium; 4Institut de recherche expérimentale et clinique (IREC), Neuro Musculo-Skeletal lab (NMSK), Université catholique de Louvain, Brussels, Belgium; 5Department of Surgery and Transplantation, Swiss HPB Center, University Hospital Zurich, Zurich, Switzerland.

Introduction: Brief bubble, and subsequent surface oxygenation is an alternative oxygenation technique for membrane-oxygenated kidneys during HMP. The aim of this study was to evaluate the metabolic effect of interruption of surface oxygenation (mimicking organ transport) during HMP as compared to continuous surface and membrane oxygenation in a pig kidney ex vivo preservation model.

Methods: A kidney of a ±40 kg pig was exposed to 30 minutes of warm ischemia and preserved according to one of the following study groups: 1) 22h HMP+intermittent surface oxygenation (30 min at start, 4h interruption followed by 17h30 surface oxygenation) during 22h HMP (n=12), 2) 22h HMP+continuous membrane oxygenation (n=6), and 3) 22h HMP+continuous surface oxygenation (n=7). Brief O2 uploading of the perfusion fluid before kidney perfusion was obtained either by a hollow fiber membrane oxygenator (study group 2) or by direct bubble oxygenation (study group 1 and 3).

Results: O2 uploading of the perfusion fluid by minimum 15 minutes of direct bubble oxygenation was as efficient as membrane oxygenation to achieve pO2 levels above 450-500 mmHg (at 4°C) before connecting the kidney to the perfusion device (Figure 1). Metabolic analysis (i.e. lactate, succinate, glutamate, ATP, ADP, AMP, NADH, NAD+ and Flavin Mononucleotide (FMN)) on end-preservation cortical and medullar tissue biopsies demonstrated a similar mitochondrial protection/preservation in all study groups (Figure 2). FMN measurement by fluorescence demonstrated no difference between all study groups during the first 270 minutes of preservation, however perfusate FMN levels were significantly higher at the end of the preservation period in the membrane-oxygenated groups as compared by both surface-oxygenated HMP groups.

Conclusion: Brief bubble and intermittent surface oxygenation of the perfusate during standard HMP at procurement site might be an effective, user-friendly, and less expensive preservation strategy to protect mitochondria when compared with membrane-oxygenated kidneys eliminating the need for a membrane oxygenator and oxygen source during transport.
212.9
Preservation Solutions for Static Cold Storage in DCD and DBD Liver Transplantation in the United States
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Static cold preservation remains the cornerstone for storing donor livers following procurement, however, the choice between University of Wisconsin (UW) and histidine-tryptophan-ketoglutarate (HTK) solutions remains controversial. Recent ILTS guidelines have recommended avoiding HTK solution for donation after circulatory death (DCD) grafts based on older reports. We studied the latest US adult graft outcomes in 3 recent eras (2006-2010; 2011-2015; 2016-2020) comparing HTK and UW solutions among 5,956 DCD LTs: 3,873 (65.0%) used UW and 1,944 (32.7%) used HTK; and 82,679 donation after brain death (DBD) liver transplantations (LTs): 63,511 (76.8%) used UW and 15,855 (19.2%) used HTK. The HTK group had higher 1- and 5-year graft survival rates of 89.7% and 74.3%, respectively, compared with 85.9% and 70.8% in the UW group in the 2016-2020 era (p=0.005). This difference remained when adjusted for important potential confounders (HR 0.78, 95% CI: 0.60, 0.99). There were no differences between groups among DCD LTs in the earlier eras, and among DBD LTs in all eras (all p-values>0.05). The latest US data suggests that HTK is at least non-inferior to UW for preserving DCD livers. These data support HTK use in DCD LT and contradict ILTS guidance.

213.1
Pediatric Donation After Cardiac Death (DCD) Livers Transplanted in Adult Recipients—Appropriate Utilization or Missed Opportunity for Waitlisted Children?
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Introduction: Donation after cardiac death (DCD) donors are increasingly recognized as an important source of donor livers. Pediatric DCD donor livers have been used successfully in pediatric recipients although this remains an uncommon occurrence. More frequently, pediatric DCD livers are used in adults. We examined outcomes of pediatric DCD livers in pediatric and adult recipients.

Methods: The UNOS STAR file was accessed to determine all patients transplanted with a pediatric DCD liver between 2007-2020. A pediatric donor was defined as one who was under 18 years of age at time of donation; a pediatric recipient was defined as a patient under 18 years of age at the time of transplantation. Donor and recipient demographic data were examined, and a p value < 0.05 was considered to be significant.

Results: 473 pediatric DCD livers were utilized over the study period. 449 (95%) were transplanted into adult recipients (P-A), while 24 (5%) were transplanted into pediatric recipients (P-P). P-P donors were younger when compared to P-A donors (6.0 vs. 13.8 yrs, p<0.05), had a lower BMI (18.4 vs. 22.3, p<0.05), longer cold storage time (7.9 vs. 6.2 h, p<0.05), and a greater distance to transplant center (279.8 vs. 118.4 miles, p<0.05). Donor gender and ethnicity were similarly distributed. There were no significant differences between both groups in final donor AST levels, ALT levels or macrosteatosis content. Three P-P recipient experienced allograft loss secondary to hepatic artery thrombosis (HAT) (12.5%), and there was no allograft loss from biliary complications or primary nonfunction (PNF). In the P-A group, 8 allografts were lost due to HAT (1.8%), 5 from biliary complications (1.1%), and 6 as a result of PNF (1.3%). Allograft survival was significantly better in P-P when compared to P-A (p=0.02).

Conclusion: Utilization of pediatric DCD liver allografts is an uncommon occurrence; however, outcomes are excellent in pediatric and adult recipients. It is interesting to note that feared complications, such as biliary complications and primary nonfunction, were not present in the P-P cohort. Utilization of pediatric DCD allografts into appropriate pediatric recipients yields good outcomes and should be strongly considered.
Preliminary Results of the First Clinical Trial to Prevent Graft Rejection in Heart Transplant Children Employing a Cellular Therapy With Autologous Treg Obtained From Thymic Tissue (thyTreg)

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Introduction: Immune allograft rejection remains the main obstacle to successful transplants. Due to their suppressive capacity, regulatory T cell (Treg) therapy is a very promising alternative to prevent rejection and achieve indefinite graft survival. Several clinical trials conducted in adults with peripheral blood Treg demonstrate the safety of the therapy, although its efficacy seems to be limited. To overcome the current barriers and make this therapy effective, we explore a pioneering strategy that employs, as an alternative source of Treg cells, the thymic tissue discarded in pediatric cardiac surgeries.

Materials and methods: We developed a novel GMP-compatible protocol to obtain large numbers of Treg cells from pediatric thymic tissue (thyTreg) suitable for use in humans. After confirming the high quality of our therapeutic product and completing preclinical studies, we have started the first worldwide phase IIa clinical trial (NCT04924491) that evaluates the safety, feasibility and efficacy of autologous thyTreg in preventing rejection in children undergoing heart transplantation. We employ the thymic tissue removed in heart transplantation surgery to produce therapeutic doses of GMP thyTreg. At day +8±2 post-transplant, a single dose of fresh autologous thyTreg is administered to the patient intravenously (randomized to 10x10^6 or 20x10^6 cells/kg), and the remaining thyTreg are cryopreserved. Patients receive their usual immunosuppressants regime (tacrolimus, mycophenolate, short-term corticosteroids) and are clinical and immunological followed up to 2 years post-transplant. A cohort of heart transplant children receiving the same immunosuppressive regime without thyTreg administration is also recruited as the control group.

Results: To date, 4 patients have received a thyTreg dose. The four thyTreg products infused showed very high viability (>94%) and purity (CD25+FOXP3+) ≥85% in all cases. The procedure’s safety is confirmed, and the preliminary results obtained in the children treated with this therapy are very encouraging. These results suggest that with a single infusion of thyTreg it is possible to maintain the reserve of Treg cells crucial to prevent rejection, even in these patients who have undergone thymectomy and treated with immunosuppressive therapy. Furthermore, so far, we have yet recruited six more patients in the trial who are still on the heart transplant waiting list, completing the 10 patients planned for this clinical trial.

Conclusion: ThyTreg cell constitutes a new therapeutic strategy to prevent rejection in children who have received heart transplants. Preliminary results of our clinical trial confirm the approach’s safety and suggest that it can preserve the peripheral Treg pool. We are confident that the improved quality and amount of thyTreg obtained with this protocol could be a step to induce immunological tolerance and thus achieve the indefinite survival of the transplanted organ.

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213.3

Long-term Outcome and Complications in Pediatric ABO-incompatible Living Donor Kidney Transplantation With rituximab Induction: A Multi-centre Investigation From the Nordic Paediatric Renal Transplantation Study Group

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Introduction: ABO-incompatible (ABOi) living donor kidney transplantation (LDKT) in adults has become routine practice at many centers worldwide. Pediatric ABOi LDKT has nonetheless remained a relatively rare event and reports on outcome following pediatric ABOi LDKT using rituximab induction are few. With the aim of evaluating long-term results and complications of pediatric ABOi LDKT, using a protocol based on antigen-specific immunoadsorption and rituximab, we undertook a retrospective multi-center study within the Nordic Paediatric Renal Transplantation Study Group (NPRTSG), comparing pediatric ABOi LDKT with ABO-compatible (ABOc) pediatric kidney transplantations with both living and deceased donors.

Material & Methods: Data was retrieved from the Scandiatransplant registry, the NPRTSG registry and medical records. In total, 6 out of 11 NPRTSG centers performed pediatric ABOi kidney transplantation (recipient age <16 years) during the study period (2003-2018). Data is currently available for 337 patients: 32 (9.5%) ABOi LDKT, 73 (21.7%) ABO-compatible (ABOc) deceased donor kidney transplantations (DDKT) and 232 (68.8%) ABOc LDKT. A case-cohort analysis of graft survival, patient survival, complications and measured GFR was undertaken.

Results: Mean follow-up was 9.2 years (±4.6 years). Patient survival at 10 years was 100% in the ABOi group, 97.2% in ABOc LDKT group and 93.5% in the DD group (p=ns). Graft survival was higher in the ABOi group compared with the other two groups (Figure 1.). The length of first hospitalization did not differ (mean 19.6 ± 12.9 days), neither did the incidence of any medical, surgical, or infectious complication during first stay (52.1% overall) (p=0.68). More episodes of acute rejection were observed during the first year in the ABOi LDKT group and the ABOc DDKT group (overall 18.4%, p=0.03). Although, no higher incidence of antibody-mediated rejection was observed in the ABOi LDKT group. First year unscheduled readmissions were more frequent in the ABOi group (74.2%) and the DDKT group (68.8%) compared with the ABOc LDKT group (62.7%, p=0.01). Graft function using measured GFR did not differ in any of the groups during the first 5 years (overall 71±25, 63±20, 56±25 ml/min/1.73 at 1, 3 and 5 years). In the ABOc LDKT group, 13 (6%) were diagnosed with malignancy during the study period compared with none in the other two groups (p=0.06).

Conclusion: Our findings suggests that pediatric ABOi LDKT is comparable to ABOc LDKT and superior to DD kidney wait listing. We did not observe any significant increase in mortality, graft failure or complications. In fact, graft survival was the highest in the ABOi LDKT group and the incidence of malignancy 0%. ABO-incompatibility should therefore not impede living donation. Finally, if the favorable outcome of ABOi LDKT is ascribed to a protective effect of rituximab induction in pediatric patients calls for further investigation.

213.4

Single-dose Rituximab Induction May Prevent EBV Viremia in Paediatric Kidney Recipients Long-term: An Investigation From the Nordic Paediatric Renal Transplantation Study Group

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Background: In 2003 we introduced the B-cell depleting agent rituximab as induction therapy for paediatric immunologic high-risk kidney transplantsations (KT). Still, the use of rituximab induction has been limited and primarily restricted to ABO-incompatible KT. In adults, rituximab induction has been evaluated in two placebo-controlled trials as prophylactic anti-rejection therapy in KT (Tydén 2009 & van Hoogen 2015). However, although rituximab appeared safe, none of these studies could prove any clear benefit of the agent within 180 days of follow-up. In paediatric KT no such prospective trial has been performed. In fact, little has been reported on rituximab induction in paediatric organ transplantation. With the aim of evaluating long-term effects of rituximab induction, we conducted a retrospective multi-centre study within the Nordic Paediatric Renal Transplantation Study Group (NPRTSG), comparing paediatric KT with and without rituximab induction.

Methods and Materials: Relevant data was retrieved from the Scandiatransplant registry, the NPRTSG registry and the electronic medical records. Six out of 11 NPRTSG centres had used rituximab induction in paediatric kidney transplantation (recipient age < 16 years) during the study period (2003-2018). A complete set of data was available for 240 paediatric first-time kidney recipients and further analysed, 27 (11%) with single-dose rituximab induction (RIT group) and 213 (89%) without rituximab induction (NoRIT group). A thorough analysis of outcome long-term including infections and other complications was undertaken.

Results: Follow-up was 9 years (± 4.4) overall. Patient survival in the RIT group was 100% at 10 years compared with 96.8% in the NoRIT group (p=ns) and graft survival 92.9% in RIT group compared with 84.6% in the NoRIT group (p=ns). In the RIT group 30.8% of patients were treated for acute rejection first year vs. 15.6% in the NoRIT group (p=0.09). EBV serologic mismatch status did not differ significantly between groups (41% overall). EBV mismatch was however associated with EBV viremia in the NoRIT group (OR 4.1) (p<0.001). No patient (0%) in the RIT group was diagnosed with EBV viremia within 36 months of KT. The incidence of CMV and BK viremia was similar in the two groups. Seven patients (3.3%) in the NoRIT group were diagnosed with malignancy during follow-up (5 with PTLD) compared with no one in the RIT group.

Conclusion: Based on the findings in this study, we conclude that single-dose rituximab induction in paediatric KT appears safe and to effectively prevent EBV viremia long-term. We therefore postulate that rituximab induction could be a forceful strategy to significantly reduce the risk of PTLD in paediatric solid organ recipients. Yet, in line with RCTs in adult KT, rituximab may have limited potential as inhibitor of early acute rejection. To fully appreciate the effects of rituximab induction in paediatric KT, prospective trials are needed.

213.5

The Potential Role of HLA Molecular Mismatch in Biopsy-proven Rejection in Pediatric Liver Transplantation

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Introduction: Tacrolimus dose adjustment most commonly based on its trough concentrations (FKCo) is fundamental to prevent graft rejection. Risk factors including HLA histocompatibility are documented in several solid organ transplants except in liver transplantation. Moreover, molecular HLA eplet mismatch (eMM) has demonstrated its superiority as a biomarker for the immunological risk stratification but scarce data is available in pediatric liver transplantation. Our aim was to evaluate the correlation between HLA eMM, FKCo variability and the interaction of both variables as risk factors for biopsy-proven acute rejection (BPAR).

Methods: Pediatric patients transplanted between 2018 and 2021 at our hospital were included and prospectively followed. Liver-graft recipients and donor pairs were HLA-typed by Next Generation Sequencing, and the number eMM for every loki was quantified using the HLAMatchmaker version of HLA Fusion software 4.6. Tacrolimus variability was calculated using the percent coefficient of variation (CV%) and tortuosity. The percent of CO above the minimum threshold at each window of time after transplantation was also calculated (Cat). Demographic, clinical, and pharmacological covariates were included in univariate (p<0.2) and Cox multivariate models. ROC analysis was performed to identify specific thresholds for BPAR development in the variables retained in the multivariate model. Kaplan-meier curves for the BPAR-free survival according to the thresholds obtained in the ROC analysis were constructed. For variables retained in the multivariate model, Fisher’s exact test was performed.

Results: Fifty-two of the 117 enrolled patients with a mean (range) age of 1.5 years (0.5-17.3), had full available data and were on tacrolimus as primary immunosuppression. Patients were followed for a mean of 350 days (range: 36-1025). BP, FKCo-free survival was 75.2% (95% CI, 63.7-88.7) and 62.7% (95% CI, 49.1-80.0) at 1 and 2 years post-transplant, respectively. Tacrolimus tortuosity (HR 1.14, 95% CI, 0.92-1.41; p=0.15) and HLA-DQ eMM (HR 1.14, 95% CI, 1.03-1.30; p=0.013) were significant risk factors for BPAR. Having a tacrolimus tortuosity ≥1.1 (sensitivity 50%, specificity 79.4%; AUC=0.59) and HLA-DQ eMM load ≥5 (sensitivity 72%, specificity 44.1%; AUC=0.59) was considered high tortuosity and high HLA-DQ eMM load according to ROC curves, respectively. Patients with low HLA-DQ eMM load and low tacrolimus variability were as likely to develop BPAR as those with high variability. However, patients with high HLA-DQ eMM load and high tortuosity (12/32) showed a higher proportion of BPAR (n=8) compared to those with high HLA-DQ eMM and low tortuosity (20/32) that developed BPAR (n=5; p=0.03).

Conclusion: Tacrolimus variability and HLA-DQ eMM were identified as risk factors for BPAR. Patients with high HLA-DQ eMM load are less likely to tolerate high tacrolimus variability without developing BPAR compared to those with low HLA-DQ eMM load.

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213.6

Arterial Stiffness and Changes in Blood Pressure: Longitudinal Analyses in Pediatric Kidney Transplant Recipients

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Background: Cardiovascular events account for 25% of deaths in children undergoing kidney transplantation (KTx). In KTx population, mortality due to cardiovascular causes is even higher than due to non-functioning graft. Pulse wave velocity (PWV), a measure of arterial stiffness, is highly predictive of major cardiovascular events and mortality. While a strong dependency between PWV and blood pressure (BP) is established, the effect of dynamic BP change on PWV has not been explored. We aimed to determine to which extent BP changes contribute to an increase in arterial stiffness, and secondly, to evaluate the importance of immunosuppression on BP in children after KTx.

Methods: We included 70 children (n=43 males) from a longitudinal prospective study with biannual visits at three German pediatric nephrology units (Essen, Hamburg-Eppendorf, Hannover). All participants were ≥2 years post-transplantation with at least two PWV measurements. Changes of systolic (ΔSBP) and diastolic BP (ΔDBP) from the baseline values were classified into “stable/decreasing”, “1-10mmHg increase”, and “>10mmHg increase”. Linear mixed models for PWV z-score (PWVz) adjusted either for ΔSBP or ΔDBP were performed. Extended analyses were performed for SBP and DBP z-scores in a dataset with monthly entries of BP, immunosuppression, and creatinine from 35 children (n=20 males, median follow-up of 74 months, person-visits n=2137).

Results: PWVz was increasing with a rate of 0.11 z-score/year (p<0.001). Compared to children with stable SBP, those with 1-10mmHg SBP or DBP increase showed a higher PWVz of 0.59 (p=0.034) or 0.86 (p<0.001), respectively. A >10mmHg BP increase was associated with an even higher PWVz (SBP: p<0.07, p=0.007; DBP: p=1.37, p=0.001). Female sex and lower eGFR were considered high tortuosity and high HLA-DQ eMM load according to ROC curves, respectively. Patients with low HLA-DQ eMM load and low tacrolimus variability were as likely to develop BPAR as those with high variability. However, patients with high HLA-DQ eMM load and high tortuosity (12/32) showed a higher proportion of BPAR (n=8) compared to those with high HLA-DQ eMM and low tortuosity (20/32) that developed BPAR (n=5; p=0.03).

Conclusion: Greater arterial stiffness is seen in patients with large BP increases and higher immunosuppressive trough levels are associated with higher DBP. This emphasizes the role of BP as modifiable risk factor for the improvement of cardiovascular outcome after transplantation.

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A Data-driven Predictive Analytics Framework for the Analysis of Prognostic Factors and Health Outcomes in Paediatric Intestinal Failure Patients

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Introduction: Machine learning (ML) involves computational methods and learning mechanisms that can help generate new knowledge from large databases. These techniques are uniquely suited to analyses of paediatric intestinal failure (IF) where classification, risk factor identification, and knowledge extraction can be challenging. Heterogeneous patient populations, small sample sizes, and variations in treatments may complicate our ability to manually identify trends in data. Factors that predict enteral autonomy (EA) and patient management (optimal intravenous lipid emulsion [ILE] solutions; central venous catheter [CVC] complications) have been described, yet a systematic approach that may be prospectively applied to large datasets has never been performed in this patient population. Our study aims to identify predictors of EA through machine learning (ML) and assess their impact on TPN duration. For patients on TPN, assessments of lipid emulsion (ILE) and central venous catheter (CVC) type were also performed.

Methods: Demographics, procedures, and outcomes for patients (N=17) from McMaster Children’s Hospital’s (MCH) Intestinal Rehabilitation Program (1999-2021) were collected for a retrospective chart review. Predictors of EA status were obtained using a decision tree ML model. Performance was evaluated as area under the receiver operator characteristics (AUC) and precision-recall (PR) curves. These predictors were assessed for ability to impact TPN duration with Kaplan-Meier (KM) estimates and Cox proportional-hazards (CPH) models. ILE treatments were compared using the Mann-Whitney U test, and CVC types were compared with KM, CPH, and analysis of variance (ANOVA).

Results: The model retrieved 10 predictors of EA status. AUC and PR curves were 91% and 71% respectively. Of these 10 predictors: sex, serial transverse enteroplasty (STEP) procedure, ileocecal valve (ICV) presence, and remnant small bowel length were significant for predicting EA status under KM, but not CPH. For ILE treatment, patients on SMOF Lipid® had lower total bilirubin values compared to Intralipid® at six months (4.0 versus 10.0 uMol/L). Longevity of peripherally inserted central catheters (PICC) was 847 days versus 268 days for tunnelled CVCs, and 181 days for ports (95% CI: 0-2044, 93-443, 144-218). Types of complications were not significantly different across CVC.

Conclusions: Our study supports the role for ML frameworks in advanced pattern recognition, and promoting adaptive clinical management. Validation of this model using our single-centre dataset supports similar conclusions derived from larger, multi-center registries. Ongoing use of our ML framework offers a potential contribution to intestinal failure analyses by helping identify unique risk factors and protective factors for EA, and approaches to clinical management in the paediatric IF population.
Systematic Use of Magnetic Double J Stent in Paediatric Kidney Transplantation: A Single Centre Experience

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Background: The intraoperative insertion of a double-J-stent (DJS) is known to reduce urological complications and is broadly accepted in kidney transplant (KTx) patients. The magnetic ureteral DJS (mDJS) represents a valid alternative device as it can be removed without cystoscopy, using a transurethral magnet. This is of particular importance in the paediatric population, as cystoscopy usually requires general anaesthesia that has been linked to later development of learning disability. To date few data are available on the systematic use of mDJS in paediatric patients undergoing KTx.

Methods: We report a retrospective analysis of 32 consecutive paediatric patients undergoing kidney transplantation at our centre from July 2020 to December 2021. Patients’ characteristics reported in table 1.

Results: Ureteral stents remained in place for a median of 35 days (range 12-76 days). Non-surgical magnetic removal of the mDJS was attempted in all cases without complications. In most cases the removal procedure was performed in an outpatient clinic by a single operator with no need for radiation. In 10 cases the mDJS were removed in the operating room under sedation before removal of the abdominal Tenckhoff catheter. All patients were clinically followed (range 3-15 months).

Conclusions: We confirm the safety and feasibility of systematic use of mDJS in the setting of paediatric kidney transplantation. The systematic use of this device contributes to reduce the need for general anaesthesia, the rate of hospital admission as well as radiation exposure. All the above likely reflect the superior outcomes observed among preemptive kidney transplant recipients, compared with transplantation following a period of dialysis, are unknown. Selection for pre-emptive transplantation of a group biased to better treatment adherence is possible. We aimed to compare medication adherence between pre-emptively transplanted young kidney transplant recipients and those who received a transplant after an interval of dialysis.

Methods: This was a secondary analysis of the Teen Adherence in Kidney transplant effectiveness of intervention trial (TAKE-IT), in which adherence was assessed with electronic monitors over a 15-month period among 11–24 year-old kidney transplant recipients. Adherence scores of 0%, 50%, or 100% were calculated for each day, depending on whether the patient took none, half, or all prescribed doses. We used ordinal logistic regression to estimate the association between pre-emptive transplantation and adherence, with generalized estimating equations to account for repeated measures within each participant. The model was adjusted for sex, age at transplant, time since transplant, primary kidney disease, race, donor source, medication insurer, household income, and adherence intervention (time-varying).

Results: There were 43 pre-emptive transplant recipients (median age 15.8 [IQR 13.7-17.6]; 60.5% male) and 103 who has been treated with dialysis (median age 15.7 [IQR 13.3-17.4]; 60.2% male). The mean adherence score was 85.1% (IQR 81.3-88.9) for those pre-emptively transplanted, and 80.0% (IQR 76.7-83.4) for those transplanted after dialysis. Table 1 shows the results adjusted logistic regression model. Preemptively transplanted recipients had significantly higher odds of adherence than those dailysed before transplantation (OR 1.76 95%CI 1.21-2.55; p=0.003).

Conclusions: Pre-emptively transplanted patients showed significantly better adherence than those treated with dialysis before transplantation. This suggests that the superior outcomes observed among preemptive kidney transplant recipients likely reflect selection of patients more likely to adhere to therapy.

Table 1. Patients’ characteristics

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender [male/female] (%)</td>
<td>17/15 (53%/47%)</td>
</tr>
<tr>
<td>Age(years) [median + range]</td>
<td>12.1 (2.0 – 17.2)</td>
</tr>
<tr>
<td>Recipient weight (kg) [average + range]</td>
<td>31.9 (8.7 – 66.8)</td>
</tr>
<tr>
<td>Cause of end-stage renal disease (#)</td>
<td></td>
</tr>
<tr>
<td>Nephrological</td>
<td>12</td>
</tr>
<tr>
<td>Urological</td>
<td>11</td>
</tr>
<tr>
<td>Others</td>
<td>9</td>
</tr>
<tr>
<td>Donor</td>
<td></td>
</tr>
<tr>
<td>Deceased</td>
<td>21 (66%)</td>
</tr>
<tr>
<td>Living Donor</td>
<td>11 (34%)</td>
</tr>
<tr>
<td>Pre-emptive transplantation [#] (%)</td>
<td>7 (22%)</td>
</tr>
<tr>
<td>Patients on dialysis before KTx [#] (%)</td>
<td>24 (75%)</td>
</tr>
<tr>
<td>Type of dialysis</td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>14 (56%)</td>
</tr>
<tr>
<td>Peritoneal</td>
<td>10 (32%)</td>
</tr>
<tr>
<td>Stents in place [week] (median + range)</td>
<td>5 (2 – 11)</td>
</tr>
</tbody>
</table>

Variable | OR (95% CI) for adherence [vs non-adherence] by electronic monitoring |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-emptive transplant (vs post dialysis)</td>
<td>1.76 (1.21,2.55); p=0.0028</td>
</tr>
<tr>
<td>Treatment intervention period (vs no intervention)</td>
<td>1.41 (1.04,1.91); p=0.03</td>
</tr>
<tr>
<td>Male (vs female)</td>
<td>1.09 (0.78,1.52); p=0.61</td>
</tr>
<tr>
<td>Age at transplant (years)</td>
<td>0.98 (0.91,1.06); p=0.59</td>
</tr>
<tr>
<td>Time since transplant (years)</td>
<td>1.03 (0.93,1.13); p=0.43</td>
</tr>
<tr>
<td>Primary disease (vs. Other)</td>
<td></td>
</tr>
<tr>
<td>CMV1 (congenital anomaly of kidney and urinary tract disease)</td>
<td>0.83 (0.57,1.22); p=0.35</td>
</tr>
<tr>
<td>PSS</td>
<td>0.93 (0.57,2.50); p=0.76</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>1.92 (1.17,3.18); p=0.01</td>
</tr>
<tr>
<td>Ancestry (vs. European)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>0.48 (0.30,0.77); p=0.0015</td>
</tr>
<tr>
<td>Other</td>
<td>1.5 (0.99,2.37); p=0.05</td>
</tr>
<tr>
<td>Using donor (vs. deceased)</td>
<td>1.08 (0.77,1.52); p=0.66</td>
</tr>
<tr>
<td>Insurer (vs. U.S. public)</td>
<td></td>
</tr>
<tr>
<td>U.S. private</td>
<td>0.00 (0.00,2.35); p=0.80</td>
</tr>
<tr>
<td>Canada provincial</td>
<td>0.99 (0.63,1.59); p=0.09</td>
</tr>
<tr>
<td>Household income (vs $25,000)</td>
<td></td>
</tr>
<tr>
<td>$25,000-50,000</td>
<td>0.77 (0.49,1.20); p=0.23</td>
</tr>
<tr>
<td>$51,000-75,000</td>
<td>1.11 (0.61,2.08); p=0.72</td>
</tr>
<tr>
<td>$76,000-100,000</td>
<td>0.77 (0.38,1.60); p=0.51</td>
</tr>
<tr>
<td>$100,000+</td>
<td>0.80 (0.48,1.33); p=0.57</td>
</tr>
<tr>
<td>unknown</td>
<td>0.83 (0.36,1.92); p=0.90</td>
</tr>
</tbody>
</table>
214.1 Strategies to Achieve Long-term Insulin Independence Using a Multimodal Approach to Beta-cell Replacement in Patients With Type I Diabetes

Steven Wise1, Miguel Nunez2, James M Gardner2, Giulia Wonner2, Garrett R Roll2, Shared M Syed2, Gregory Sztot2, Medhi Tokhoji2, Kristina Johnson2, Umesh Masharani2, Andrew M Possett2, Peter G Stock2, 1Comprehensive Transplant Center, Cedars-Sinai Medical Center, Los Angeles, CA, United States; 2Division of Transplantation, University of California, San Francisco, San Francisco, CA, United States.

Purpose: Beta cell replacement, via islet or solid organ pancreas transplant, remains the best strategy to restore insulin independence in patients with Type 1 diabetes mellitus (T1DM). Insulin independence beyond ten years is limited, with calcineurin inhibitors (CNI) contributing to beta cell toxicity and impairing renal function. Here, we report long-term results for multimodal beta cell replacement including islet and pancreas after islet (PAI) transplant with CNI-free immunosuppression (IS) regimens based on Belatacept (BELA) and Efalizumab (EFA).

Methods: Ten non-uremic patients with severe T1DM received their first islet cell transplant between 2007 and 2009 with CNI-sparing IS based on BELA (n=5) or EFA (n=5). Patients were monitored for a mean of 12.9 ± 1.1 years from islet transplant for beta cell function and renal function. Following islet failure, patients were considered for repeat islet infusion and/or PAI transplant. Circulating immunologic phenotype was characterized in the first year.

Results: Seven of 10 patients (70%) maintained insulin independence with normalization of HbA1c (3 BELA, 4 EFA) at 10 years post-islet transplant; four patients (2 EFA, 2 BELA) achieved long-term insulin independence after one islet infusion and three additional patients (2 BELA, 1 BELA) following PAI transplant (Figure 1, Figure 2). Six of 10 (60%) remain insulin independent currently, at a mean follow-up of 13.3 ± 1.1 years from 1st islet infusion. Eight of 10 patients (80%) achieved stage 3a CKD and without progression to stage 4 or 5 CKD (Figure 2). One patient progressed to stage 5 CKD after islet failure and return to full insulin dependence. Patients receiving EFA demonstrated profound expansion of circulating CD4+Foxp3+ regulatory T cells (Tregs). One patient (EFA-4) demonstrated Tregs comprising 68% of all circulating CD4+ T cells, and remains insulin independent despite discontinuing all immunosuppression, thus demonstrating the first reported case of operational tolerance in islet transplantation.

Conclusions: Our results describe a multi-modal, personalized approach to beta-cell replacement. In our series, repeat islet transplant is ineffective at maintaining long-term insulin independence. PAI results in durable insulin independence but is associated with deterioration of renal function secondary to CNI dependence. EFA-based immunosuppression resulted in significant expansion of Tregs following transplantation, with one islet recipient establishing operational tolerance.

214.2 Impact of TNF Alpha Inhibitor Induction Therapy on Graft Thrombosis Following Pancreas Transplantation

Benoit Meenard1, Delphine Korvel1, Thomas Prudhomme1, Georges Karam1, Julien Branchereau1, Diego Cantarovich1, 1Institute of Transplantation-Urology-Nephrology, Nantes University Hospital, Nantes, France.

Introduction: Transplant thrombosis is the main cause of early pancreas failure. Factors related to the donor, to the recipient (theological disorders, overweight) and a prolonged cold ischemia time are associated thrombosis which seems to be linked to transplant pancreatitis. Tumor necrosis factor alpha inhibitor (TNFi), has anti-inflammatory properties which could reduce transplant pancreatitis and consequently the rate of venous thrombosis. We prospectively evaluated the safety and efficiency of TNFi induction therapy on the rate of venous thrombosis.

Methods: TNFi was introduced into clinical practice in our center in April 2017. Etanercept was administrated at day 0 (50mg), day 3, 7 and 10 (25mg) in combination to anti-thymocyte globulin, 5-day steroids, tacrolimus and mycophenolic acid. Patients with a minimum one-year follow-up were compared to patients transplanted before April 2017.

Results: Between April 2017 and December 2020, 60 pancreas transplant recipients received TNFi and were compared to the last 60 recipients transplanted before April 2017. Sociodemographic characteristics of recipients and donors were similar. Most transplantations were SPK (73%). Tolerance of Etanercept was excellent (no case of discontinuation). The rate of thrombosis in the TNFi group was 13.6% versus 25% in the control group (p=0.11). No thrombosis occurred after 1 month. One month and 1-year transplant survival rates were respectively 96.6% and 93.2% in the TNFi group and 93.3% and 88.3% in the control group (p=0.23). One month and 1-year patient survival rates were 100% in the TNFi group and 96.7% in the control group (p=0.27). The rates of CMV infections were similar in the 2 groups. No case of tuberculosis was observed.

Conclusion: The perioperative administration of TNFi in pancreatic transplantation appears to be safe and may decrease the rate of transplant venous thrombosis.
214.3

Thrombomodulin Protein Transiently Tethered To Surface of Islets Enhance Engraftment in an Intraportal Transplantation Model by Inhibiting Peri-transplant Inflammatory Reactions

Ali Turan1, Lei Zhang2, Mohammad Tariqou3, Vahap Ullker4, Ayse Ece Gulen5, Esma S. Yolcu1,2, Haval Shirwan1,2.
1Molecular Microbiology and Immunology, University of Missouri, Columbia, Columbia, MO, United States; 2Department of Child Health, University of Missouri, Columbia, Columbia, MO, United States.

Introduction: The instant blood mediated immune reaction (IBMIR) orchestrated by innate immune responses is responsible for substantial loss of islet mass following intraportal transplantation. Thrombomodulin (TM) is a multifaceted innate immune modulator that blocks mediators of coagulation, complement activation, and phagocytosis as major culprits of IBMIR. In this study, we assessed the efficacy of a novel form of TM in mitigating IBMIR in a minimal mass syngeneic islet transplantation model.

Methods: A chimeric gene containing the extracellular domain of TM with a modified form of streptavidin (SA-TM) was generated, expressed in insect cells, and protein was characterized for structure and function. SA-TM was tethered to the surface of islets modified with biotin exploiting the high affinity between biotin and streptavidin (SA). SA-TM function was tested on neutrophils and macrophages in vivo and in vitro. Engineered islets were evaluated for viability and function as well as mitigating IBMIR ex vivo and in vivo. Intraportal transplantation was performed with 200 islet equivalents using streptozotocin-diabetic syngeneic recipients (n=7). SA protein was used as a control (n=6). Animals were monitored for blood glucose and graft function was assessed using an intraperitoneal glucose tolerance test. Flow cytometry and transcriptomic analysis were performed on graft recipients various time points post-transplantation.

Results: Islets were effectively engineered with SA-TM without a major impact on their viability and function. SA-TM prevented NETS formation of cells, and protein was characterized for structure and function. SA-TM was tethered to the surface of islets modified with biotin exploiting the high affinity between biotin and streptavidin (SA). SA-TM function was tested on neutrophils and macrophages in vivo and in vitro. Engineered islets were evaluated for viability and function as well as mitigating IBMIR ex vivo and in vivo. Intraportal transplantation was performed with 200 islet equivalents using streptozotocin-diabetic syngeneic recipients (n=7). SA protein was used as a control (n=6). Animals were monitored for blood glucose and graft function was assessed using an intraperitoneal glucose tolerance test. Flow cytometry and transcriptomic analysis were performed on graft recipients various time points post-transplantation.

Conclusion: Transient display of SA-TM on the surface of islets is an effective approach to modulate innate immune pathways involved in early islet graft loss with implications for autologous and allogeneic islet transplantation.

NIH U01AI132817. R01AI121281.

214.4

The Genetic Epidemiology of Hereditary Pancreatitis in Australia and Its Effect on Patients of Total Pancreatectomy and Islet Auto Translation (TP-IAT)

Denghao Wu1,2, Christopher Drogermüller1,2, Richard Couper1,2, David Torpy1,2, Hamish Scott1,3, Lyle Palmer1, Sunita De Sousa1,2,3, Patrick Toby Coates1,2.
1School of Medicine, University of Adelaide, Adelaide, Australia; 2Kidney and Islet Transplantation, Royal Adelaide Hospital, Adelaide, Australia; 3Centre for Cancer Biology, SA Pathology, Adelaide, Australia.; Centre for Clinical and Experimental Transplantation.

Introduction: Hereditary Pancreatitis (HP) is a cause of pancreatitis in childhood leading to lifelong disability and an elevated risk of pancreatic cancer. The clinical and genetic features of HP have not been characterised in Australia. This project aims to understand the effects of HP-associated variants on disease risk and progression, and their pertinence on past and future patients of TP-IAT.

Methods: HP patients were identified from existing hospital records. Interviews were administered to collect HP-associated data including pain management, medical prescriptions, interventions, smoking and alcohol history, and overall quality of life. Saliva samples were obtained for whole-exome-sequencing (WES). Genetic data were analysed using standard bioinformatics toolkits for variant discovery and correlation with HP phenotype. This was compared to a control sample of 2,504 patients with adult-onset chronic pancreatitis.

Results: A total of 44 HP patients from 10 independent pedigrees were identified. Eighty-four percent of HP patients reported ongoing opioid use to control pain and 79% of patients reported ongoing moderate to severe pain. The majority (57%) of the HP cohort self-identified as Indigenous Australians and HP was 67 times more prevalent in Indigenous populations than non-Indigenous. Overall, 14/16 individuals underwent TP-IAT exhibited substantial reduction in analgesic requirement. The estimated prevalence of HP in SA was 2.48 per 100,000. HP was ~67 times more prevalent in Indigenous people than non-Indigenous South Australians. The study cohort had a younger age of onset and higher female ratio when compared to 2,504 of control adult-onset CP cases.

Conclusion: Our estimated prevalence of HP is higher than previously described and disproportionately affect Indigenous populations. The percentage of HP patients requiring lifelong analgesics is alarming and genetic factors are an important cause of pancreatitis in Australian children. Finally, TP-IAT has been successful as a new therapy for HP management.
Long-term Outcomes in Primary Simultaneous Kidney and Pancreas Recipients Under Steroid Avoidance in the United States

Adam Cerise2, Scott Jackson3, Raja Kandaswamy2, Samy Riad1.
1Nephrology, University of Minnesota, Minneapolis, MN, United States; 2Surgery, University of Minnesota, Minneapolis, MN, United States; 3Complex Care Analytics, University of Minnesota, Minneapolis, MN, United States.

Background: Steroid avoidance in kidney transplantation has been proven non-inferior. Data on steroid avoidance in simultaneous pancreas-kidney (SPK) is scant.

Methods: We utilized the Scientific Registry of Transplant Recipients (SRTR) between 2000 and 2020 we studied all primary crossmatch negative SPK recipients (N=5683) who received anti-thymocyte globulin for induction and were discharged alive on tacrolimus and mycophenolate with or without steroid maintenance. Recipients were grouped according to steroid use into two groups: steroid maintenance n=4191 and steroid avoidance n=1492. Kaplan-Meier curves with generated for Recipient and allografts survival according to steroid maintenance censored at 10 years. Predictors for recipient and grafts survival were examined using Cox proportional Hazards. Models were adjusted for age, BMI, ethnicity, diabetes type, HLA-antigen mismatches, cold ischemia time, transplant era, preemptive transplantation, and PDRI with the transplant center included as a random effect.

Results: Steroid avoidance gained popularity over the years, accounting for over one fourth of the studied cohort. One-year acute rejection rates by steroid avoidance were comparable for kidney (8.6 vs. 9%, P=0.783, however pancreas rejection rate was lower in the steroid avoidance group (7.9 vs. 10%, P=0.035). In the Kaplan-Meier analysis for the pancreas death-censored graft survival (DCGS), steroid avoidance was associated with better pancreas graft survival (log-rank p =0.006). The kidney DCGS did not vary between groups (log-rank p=0.233). In the multivariable models, steroid avoidance did not influence recipient (LLCI, aHR, ULCI) (0.94, 1.15,1.39), death-censored pancreas graft survival (0.75, 0.93, 1.16) or kidney (0.95, 1.18, 1.45) compared to recipients on steroid maintenance.

Conclusion: After multivariable adjustment for recipient and grafts characteristics, steroid avoidance is associated with similar patient, pancreas and kidney grafts outcomes when compared with steroid maintenance in SPK recipients following r-ATG induction and tacrolimus plus mycophenolate maintenance.

The data reported here have been supplied by the Hennepin Healthcare Research Institute (HHRI) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government.
Outcomes in Mild Obese Recipients With Diabetes Mellitus Type 2 That Received Simultaneous Kidney Pancreas Transplant

Massini Merzkani1, Haris Murad1, Mei Wang1, Wenjun Hu1, Mengmeng Ji1, Omar Alhomar1, Obadah Alzahabi1, Yazen Al-Hosni1, Mohamad Zayed1, Jason Wellen1, Krista L Lentine2, Su-Hsin Chang1, Tarek Alhamad1.

1Washington University School of Medicine at St.Louis, Saint Louis, MO, United States; 2Saint Louis University School of Medicine, Saint Louis, MO, United States.

Objective: Simultaneous pancreas and kidney transplant (SPKT) has excellent outcomes in patients with end stage renal disease secondary to diabetes mellitus type 2 (DMT2). The outcome of SPKT in DMT2 obese recipients with Body Mass Index (BMI) >30 kg/m2 has not been well studied.

Methods: We reviewed Organ Procurement and Transplantation Network (OPTN) data that had SPKT for DMT2 between 1/1/2000 and 6/12/2020. Patients with age <18 years, BMI<20 kg/m2 and ≥35 kg/m2, prior transplants (OPTN) data that had SPKT for DMT2 between 1/1/2000 and 6/12/2020. Patients with age <18 years, BMI<20 kg/m2 and ≥35 kg/m2, prior transplants were excluded. Obesity was defined as having a BMI between the ranges 30.0-35.0 kg/m2 and lean recipients with BMI 20.0-29.9 kg/m2. The outcomes were kidney and pancreas graft loss and death at post-SPKT 1, 5, 10 years, and the entire follow-up. The association of obesity with each outcome was analyzed using multivariable Cox regression including adjustment for recipient, donor, and transplant characteristics.

Results: A total of 1,311 SPKT with DMT2 were analyzed. Obesity in SPKT recipients with obesity and DMT2 were not at increased risk of death aHR=0.97, 95% CI[0.66-1.43] at all follow-up time points.

Conclusion: SPKT recipients with obesity and DMT2 were not at increased risk of death and kidney or pancreas allograft failure. This study encourages many centers to not exclude patients with DMT2 with obesity for SPKT, which can benefit survival and decrease DM complications.

Impact of Hypothermic Oxygenated Perfusion (HOPE) on Endothelial Cell Biology in a Preclinical Porcine Model of Pancreatic Transplantation

Benoit Mesnard1,2, Sarah Bruneau2, Thomas Prudhomme2, Etohan Ogbemudia3, Delphine Kervella2, Stéphanie Le Bas-Bernard2, David Minault2, Jéremy Hervouet2, Jérôme Rigaud1, Lionel Badet4, Gilles Blanchot5, Julien Branchereau1,2,3.

1Department of Urology and Transplantation Surgery, Nantes University Hospital, Nantes, France; 2Institut de Transplantation Urologie Néphrologie (ITUN), Centre de Recherche en Transplantation et Immunologie (CRTI) UMR 1064, INSERM, Nantes, France; 3Nuffield Department of Surgical Science, University of Oxford, Oxford, United Kingdom; 4Department of Urology and Transplant Surgery, Hôpital Edouard-Herriot, Hospices Civils de Lyon, Lyon, France.

Introduction: Hypothermic Oxygenated machine PErfusion (HOPE) is under investigation in kidney and liver transplant to improve the security and outcomes of transplants from marginal donors. The effect of HOPE on endothelial cell biology has been poorly studied in organ transplantation and to date no studies have evaluated it in pancreatic transplantation. We propose to evaluate the effect of HOPE versus statical cold storage on endothelial cell biology of pancreatic transplants during hypothermic storage.

Method: We set up a model of marginal donors with a donation after circulatory death in an animal house porcine model (warm ischemia = 30 minutes). After pancreas procurement, pancreatic transplants were preserved during 24 hours in hypothermic condition either in statical cold storage (SCS) (n=2) or on HOPE (Waves machine, Institute Georges Lopez) with an oxygenation at 95% at 2L/min (n=2). A perfusion pressure of 15mmHg. Surgical biopsies were performed after organ removal and after 3 and 24 hours of storage. Effects on endothelial cell biology were assessed by quantitative RT-PCR (RT-Profiler PCR Array, Qiagen). The expression of 84 genes involved in permissibility and vessel tone, angiogenesis, cell adhesion, inflammation and apoptosis were evaluated.

Results: The analysis of the associated markers of vascular endothelial function expression highlighted an overexpression of markers of inflammation, cell adhesion, and apoptosis during static preservation for 3h and up to 24h of preservation.

Conclusion: Our results suggest that HOPE may influence endothelial cell biology during preservation by decreasing markers related to inflammation and apoptosis.

The authors thank The French association of Urology, Nantes Université and the Agence of Biomedicine for their financial support and the Institut Georges Lopez for the material support.
Pancreas Transplantation From Cardiac Death Donors Versus Neurological Death Donors at a Tertiary Care Center

Catherine Parmentier, Michael Bleszynski, Samrat Ray, Andrea Norgate, Gonzalo Sapiochen, Ian McGilvray, Anila Yousuf, Markus Selzner, Trevor Reichman.

1Multi Organ Transplant Department, University Health Network - Toronto General Hospital, Toronto, ON, Canada.

Introduction: Pancreas transplantation is the only curative treatment for patients with complicated diabetes. Donor organ shortages and strict organ allocation policies are rate limiting factors that limit potential recipients from receiving a graft. The pancreas is also the most discarded organ for transplantation further limiting suitable grafts for transplant. To meet the demands of the organ shortage, expanding the criteria for suitable pancreas donors has been explored. The program in Toronto has been using donation by cardiac death (DCD) pancreas donors for over a decade.

Methods: A retrospective study of all DCD cases (n=33) performed at Toronto General Hospital from January 2011 to December 2020 were matched 1:3 with NDD cases (96) for a total of 129 pancreas transplantations. All statistical analysis and graphs were performed using GraphPad Prism 9 software. Continuous data are presented as mean and standard deviations, categorical data as total numbers and percentages and Kaplan Meier method was used to estimate patient and graft survival. A significant P value was set to ≤0.05.

Results: Patient demographic characteristics are presented in Table 1. In both groups, the majority of the recipients were male (DCD 81.81% vs NDD 61.45%). Major cause of death was anoxia in both groups and DM1 was the principal diagnosis in pancreas allograft recipients. Simultaneous Pancreas Kidney transplantation was the most common procedure performed (DCD 87.9% vs NDD 87.6%). Graft failure and mortality were comparable between recipients of DCD and DBD grafts (p = 0.21 and p=0.42, respectively). There was no statistically significant difference in graft and patient survival for 1, 5 and 8 years between groups (Figure 1).

Conclusion: Our data suggests there is no difference in outcomes in recipients of grafts from DCD versus DBD donors. The use of DCD grafts is safe and feasible and should be encouraged to become a standard practice to meet the increasing waiting times and number of patients in need of a pancreas allograft.

<table>
<thead>
<tr>
<th>Recipient age (mean, SD)</th>
<th>DCD (n=33)</th>
<th>NDD (n=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (49.9%)</td>
<td>44.7 (± 9.4 years)</td>
<td>44.5 (± 8.4 years)</td>
</tr>
<tr>
<td>Female (50.1%)</td>
<td>44.7 (± 9.4 years)</td>
<td>44.5 (± 8.4 years)</td>
</tr>
</tbody>
</table>


Figure 1: A, 1-year graft survival; B, 5-year graft survival; C, 1-year patient survival; D, 5-year patient survival; (DCD) = Donation after Cardiac Death (DCD); (NDD) = Neurological Death Donor.
Pancreas Transplants in the Elderly Patient - How Far Can We Go?

Angelika Gruessner1, Subodh J. Saggi1, Rainer WG Gruessner1.
1Medicine, SUNY Downstate Health Sciences University, Brooklyn, NY, United States.

Background: While kidney transplantation in the elderly diabetic patient is an accepted treatment, pancreas transplants in older patients are controversial. Many centers have an age limit of 60 years or lower in place. The aim of this study was to describe the surgical risk of pancreas transplantation in the elderly and the potential life-years gained by undergoing a pancreas transplant.

Methods: Between 2000 and 2017, 885 diabetic patients 58 years of age or older were listed for a primary deceased donor pancreas transplants in the USA. 75% of patients were listed for a simultaneous pancreas kidney transplant (SPK), 12% previous kidney for a pancreas after kidney (PAK) and 12% for a pancreas transplant alone (PTA). Uni- and multivariate statistical methods were used to assess wait-list mortality, outcomes and life-years gained for older pancreas transplant recipients. Each patient had a potential follow-up of at least 4 years post-transplant.

Results: The 1- and 3-year mortality rates while waiting for a transplant were 9.6% and 32.6% for SPK, 5% and 14% for PAK, and 6.9% and 15.4% for PTA. Of these wait-listed patients, a total of 489 underwent a pancreas transplant (333 SPK,79 PAK, 77 PTA). Table 1 shows the demographics and outcomes for the 3 transplant categories. Patient and pancreas graft survival was not statistically different between the 3 transplant categories.

Conclusions: Pancreas transplants can be safely performed in older patients with excellent patient and graft outcomes. The additional gain in life-years is especially high in SPK recipients. The gain in life-years is not as high in solitary transplants because the mortality on the wait-list is not as high as in SPK patients. The mortality of patients with hypoglycemia remains high at any age and should also be an indication for pancreas transplantation in older, diabetic patients.

<table>
<thead>
<tr>
<th>Age at Tx (median &amp; range)</th>
<th>SPK</th>
<th>PAK</th>
<th>PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Male</td>
<td>64%</td>
<td>70%</td>
<td>56%</td>
</tr>
<tr>
<td>% Type 2 diabetic</td>
<td>23%</td>
<td>11%</td>
<td>5%</td>
</tr>
<tr>
<td>Wait-list Time (median &amp; range)</td>
<td>6.3 (0.3 - 69.9)</td>
<td>4.9 (0.1-36.0)</td>
<td>3.4 (0.1-50.3)</td>
</tr>
<tr>
<td>Patient Survival 1-year</td>
<td>93%</td>
<td>95%</td>
<td>93%</td>
</tr>
<tr>
<td></td>
<td>3-year</td>
<td>88%</td>
<td>92%</td>
</tr>
<tr>
<td></td>
<td>5-year</td>
<td>81%</td>
<td>75%</td>
</tr>
<tr>
<td>Pancreas Graft Survival 1-year</td>
<td>85.6%</td>
<td>91.0%</td>
<td>80.2%</td>
</tr>
<tr>
<td></td>
<td>3-year</td>
<td>80.5%</td>
<td>75.5%</td>
</tr>
<tr>
<td></td>
<td>5-year</td>
<td>73.6%</td>
<td>72.4%</td>
</tr>
<tr>
<td>Life-years gained</td>
<td>11.1 Years</td>
<td>1.8 Years</td>
<td>4.4 Years</td>
</tr>
</tbody>
</table>

215.1

Recoverability of Diabetic Nephropathy of Donor Kidney After Kidney Transplantation

Kyo Won Lee1, Jae Bem Park1, Min Jung Kim2, Sung Hae Park1, Namkee Oh1.
1Department of Surgery, Samsung Medical Center, Seoul, Korea;
2Department of Surgery, Seoul Medical Center, Seoul, Korea.

Background: Some kidney donors have diabetes, and little of their natural course of diabetic nephropathy (DN) is known. The aim of this study was to analyze the changes in pathologic lesions in the diabetic donor kidney after KT by performing biopsy 2 weeks and 1 year after KT.

Methods: This retrospective study included 103 patients who underwent KT, with kidneys from donors with a history of diabetes mellitus (DM). Among these, 37 underwent biopsy 2 weeks and 1 year after KT, of which, data of 34 patients were reviewed. Biopsy specimens were reviewed using light microscopy and electron microscopy. Glomerular basement membrane (GMB) thickness at 2 weeks and 1 year was compared.

Results: Biopsy showed that DN occurred in 29 of the 34 patients. However, 17 of them (50%) were classified as having class I, a mild case with an increase in GMB thickness. Extremely small histological changes were observed in 22 patients (64.7%), including 5 patients who did not show DN. At 1 year after transplantation, there was no change in the DN histologic class in 26 patients (76.5%), and there was no statistically significant difference in the change in GMB thickness. This pattern was observed regardless of the recipient’s DM or glucose control status.

Conclusions: Donor DN was mostly stable for 1 year after KT, and this pattern did not depend on the recipient’s DM or glucose control status. With this understanding, clinicians can use kidneys from DM donors with more comfort, thereby reducing the kidney discard rate.
215.2

Urinary Selenium Excretion and Long-term Outcomes in Stable Kidney Transplant Recipients

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Introduction: Although kidney transplantation is the best available treatment for end-stage kidney disease (ESKD), much room for improvement of long-term outcomes remains. One potential modifiable factor is the status of the essential trace element Selenium (Se), which must be obtained from diet, and is vital for promotion of antioxidant defence and inflammation regulation. Trace elements imbalance is common in patients with ESKD and on haemodialysis, and is not entirely corrected after kidney transplantation. We aimed to study whether Se status is associated with graft failure and mortality in kidney transplant recipients (KTR).

Methods: In this prospective cohort study, all adults KTR with a functioning graft for ≥1-year, without a history of addiction or malignancy, who visited the outpatient clinic of the University Medical Center of Groningen (The Netherlands) between November 2008–May 2011 were invited to participate. Twenty-four-hour urinary Se was chosen as the measurement for Se status since it is considered a trustful indicator of effective Se intake. All participants were asked to collect a 24-hour urine sample during the day before to their visit to the outpatient clinic and urinary Se was measured using inductively-coupled plasma mass spectrometry. The primary endpoints of the current study were all-cause mortality and graft failure. No participants were lost to follow-up.

The association between urinary Se and outcomes was tested by means of Cox-proportional hazards regression analyses and restricted cubic splines for graphic purposes. For analyses IBM SPSS software and R Studio were used.

Results: A total of 693 stable KTR were included (mean age 53 ± 13 years, 57% male, 96% Caucasian) at a median of 5.39 [IQR, 1.97–12.04] years after transplantation, with a mean eGFR of 52 ± 20 mL/min/1.73m2. Median 24-hours urinary Se at baseline was 18.8 [IQR,15.1-23.4] µg. During a median follow-up of 5.4 [IQR 4.8–6.1] years, 150 (21%) died and 83 (12%) developed graft failure. Multivariable-adjusted analyses showed that 24-hour urinary Se excretion was associated with a lower risk of all-cause mortality (HR 0.72; 95% CI, 0.61-0.85 per 1-SD, P<0.001) and graft failure (HR 0.74; 95% CI, 0.59-0.92 per 1-SD, P=0.007) (Figure 1). The association of all-cause mortality with 24-hours urinary Se remained independent of adjustment for age, sex, and graft function (eGFR, proteinuria and 24-hours urinary volume), while this was not the case for graft failure (P=0.01 and P=0.36, respectively).

Conclusion: In a large cohort of stable KTR, 24-hours urinary Se was lower than reported for healthy individuals. Furthermore, Se excretion was inversely associated with the risk of long-term all-cause mortality and graft failure, and the association of all-cause mortality remained independent of baseline graft function. Further studies are warranted to elucidate whether Se-targeted interventions may improve long-term outcomes in KTR.
215.3

Prediction of Post-transplant Hospitalization Among Kidney Transplant Recipients With Clinical Notes and Electronic Healthcare Record Data

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Background: Rehospitalization after kidney transplant is costly to patients and healthcare systems and is associated with poor outcomes. Prediction models have previously been used to identify patients at risk of rehospitalization with limited success. Few studies have examined the inclusion of free-text data from clinical notes in the electronic medical record (EMR) and natural language processing (NLP) techniques to enhance the prediction of rehospitalization.

Methods: In this study, we aimed to include EMR clinical notes in predictive models of 30-day rehospitalization (30DR) post-kidney transplant in a retrospective, observational study of first-time recipients of kidney transplant at a large, urban hospital in the Southeastern United States between January 2005 and December 2015 using both structured (EMR) and unstructured (i.e. clinical notes) data. We used NLP techniques on eight types of clinical notes, which were mined for possible new predictive features of 30DR post-kidney transplant and included in predictive models built with unsupervised machine-learning approaches and text mining using Term Frequency-Inverse Document Frequency (TF-IDF) methods. We built several predictive models, including structured data only and combinations of structured data with clinical notes. The area under the curve (c-statistic) was used to determine and compare model accuracy, and 5-fold cross-validation was used to test model performance.

Results: Among 2,060 kidney transplant recipients, 30.7% were readmitted within 30 days. The mean age was 51 years and 47% were Black or African American. TF-IDF identified words that most frequently appear in one clinical note but least frequently in all other documents (Figure). Predictive models had similar performance when considering structured data from the EMR only (c-statistic: 0.6821; 95% CI 0.6644, 0.6998) and combined structured + progress notes (c-statistic: 0.6902; 95% CI 0.6699, 0.7105). Predictive models built with clinical notes alone performed worse than models using structured data. Notes that improved model performance the most were more heavily clinical, including progress notes, consultation notes, and discharge summaries (Table).

Conclusions: Future multi-center studies should use more advanced NLP techniques to create novel predictors from social worker and other non-medical but important predictive notes. Researchers should also consider pooling data from multiple institutions to increase sample size.

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215.4

Examining Trends in the Survival Benefit of Re-kidney Transplantation Over the Past Three Decades

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Background and objectives: A survival benefit to re-kidney transplantation (KT) has been demonstrated and the risk profile of patients being considered for re-KT is widening. Furthermore, outcomes of patients on dialysis have improved over time for those with a history of graft failure. Thus, we tested whether the survival benefit of re-KT has diminished over time.

Methods: Using SRTR data, we identified patients 25,397 patients who underwent re-KT from 1990-2019 and 23,597 waitlisted counterfactuals from the same year with the same waitlisted time following graft failure. We assessed the survival benefit of re-KT using the sequential stratification method. We tested whether this association differed by age at listing (18-64 vs. ≥65 years), and by era of listing (1990-99, 2000-09, 2010-19; pre- vs. post-KAS era [2010-14 and 2015-19].

Results: Patients who received re-KT had a better survival than waitlisted counterfactuals (1-year:96.5% vs. 95.2%, 3-year:92.1% vs. 95.1%, 6-year:83.9% vs. 70.8%). In adjusted analyses, re-KT was associated lower hazard of mortality compared with waitlisted counterfactuals (aHR=0.62, 95%CI:0.60-0.64) and this association was not different by age at waitlisting (Pinteraction=0.30). When stratifying the analysis by era, the survival benefit of re-KT was noted in all three eras (1990-99:aHR=0.70, 95%CI:0.65-0.74; 2000-09:aHR=0.58, 95%CI:aHR=0.56-0.61; 2010-19:aHR=0.55, 95%CI:0.51-0.59) (Figure). Also, when compared with the 1990-99 era, the survival benefit of re-KT was higher in the 2000-09 and 2010-19 eras (Pinteraction=0.001 for both). Furthermore, during the KAS era, there was a survival benefit to re-KT (aHR=0.57, 95%CI:0.51-0.65) and which was higher than that observed in the pre-KAS era (Pinteraction=0.004).

Conclusion: Re-KT is associated with a significant survival benefit when compared with waitlisted patients on dialysis and over time incremental increases in the survival benefit were observed. This benefit exists for older and younger adults. We recommend examination of current practices surrounding re-KT referral and candidacy and the development of guidelines and policies to increase re-KT among patients of all ages.

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215.5

Redefining Sarcopenia: Tomographic Muscle Mass Measurements Correlated to Urinary Creatinine Excretion and Glomerular Filtration Rate

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Introduction: Determining the presence of sarcopenia is important when assessing whether a patient is fit for surgery. Imaging with computed tomography (CT) has proven to be one of the most accurate and objective methods for assessment of muscle mass, but consensus on cut-off values for sarcopenia is lacking. The purposes of this study were to assess age-, sex-, and body mass index (BMI)-specific reference values of muscle mass in a large healthy Caucasian population and to correlate skeletal muscle index (SMI) to 24-hour urinary creatinine excretion rate (24-hr UCE), estimated glomerular filtration rate (eGFR), and measured glomerular filtration rate (mGFR).

Methods: Between 2002 and 2019, 964 healthy subjects from the University Medical Center Groningen were included in this study. Skeletal muscle area (SMA) was determined from an axial CT slice at vertebral level L3 and included psoas, paraspinal and abdominal wall muscles. SMI and skeletal muscle radiation attenuation (SMRA) were analysed and subsequently age-, sex- and BMI-specific reference values were calculated. SMI was correlated to 24-hr UCE, eGFR and mGFR.

Results: Mean subject age was 53 ± 11 years and 50% were male. Subjects were stratified by sex and age. The reference values for low muscle mass (calculated as two standard deviations below the mean) of SMI in males were 38.8 cm²/m² for 20-29 years, 39.2 for 30-39 years, 39.9 for 40-49 years, 39.0 for 50-59 years, 37.0 for 60-69 years, and 36.8 for 70-79 years. For females, reference values of SMI were 37.5 cm²/m² for 20-29 years, 35.5 for 30-39 years, 32.8 for 40-49 years, 33.2 for 50-59 years, 31.3 for 60-69 years, and 31.5 for 70-79 years. 24-hr UCE and SMI were significantly correlated (r = 0.54, p < 0.001) and Bland-Altman plot showed no bias between these two methods of assessing muscle mass (mean = 0.001, SD = 0.95, p = 0.08). eGFR showed no statistically significant correlation with SMI, but SMI and mGFR were positively correlated, r = 0.46 ≤<0.001.

Conclusion: This study provides age-, sex-, and BMI-specific reference values for skeletal muscle parameters at level L3, that can be used as reference data in clinical practice and future studies assessing the presence of sarcopenia. It also shows a strong, positive correlation between CT derived SMI values and 24-hr UCE.
215.7

Conversion to Belatacept Based Immunosuppression Regimen in Kidney Transplant Patients: Lessons Learned

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Background: The costimulatory inhibitor belatacept (Bela) has been shown to be an effective alternative in several clinical situations, including calcineurin toxicity, de novo alloantibody formation and thrombotic microangiopathy. To further explore the usefulness of Bela under various clinical scenarios, we performed a retrospective analysis of a prospective database of all recipients who were converted to a belatacept maintenance immunosuppression regimen after kidney transplantation.

Methods: This single-center retrospective study reviewed the electronic records of all patients who received a KT between 2016 and 2020. A total of 57 patients were converted to Bela. Of these recipients, 25 (43.8%) converted within the first 6 months, and 32 (56.2%) converted after 6 months. The indications for conversion were: calcineurin inhibitor (CNI) toxicity (26.3%), thrombotic microangiopathy (8.8%), de novo DSA (36.8%), chronic antibody rejection (5.5%) incidence of GVHD has been achieved in mismatched recipients of living donor renal allografts (KTx). Recipients were conditioned with fludarabine (30mg/m2/dose, days -5,-4,-3, 5 cyclophosphamide (50mg/kg/dose, day-3 and+3), 200 cGy TBI (day-1) followed by KTx (day0).

A G-CSF mobilized product was apheresed from the donor, processed to remove graft-versus-host disease (GVHD)-producing cells yet retain CD34+ cells and FC, and cryopreserved until administration day+1 post-KTx. Follow up is 60 - 154 months. Pts ranged in age from 18-64 yrs and were 6/6 HLA matched related to 0/6 matched unrelated. MMF and tacrolimus immunosuppression (IS) was weaned and discontinued at 1 yr if post-Tx chimerism, normal renal fcn and normal KTx biopsy were noted.

Results: Durable chimerism allowing for full IS withdrawal developed in 26 pts (time off IS 48- 136 months; the majority (23/26) showed full (>95%) donor whole blood/T cell chimerism, 6 subjects have been IS free for > 10 years.Transient chimerism was seen in 8 pts. All stable chimeric subjects retained chimerism after removal of IS and remain rejection-free. Long term chimeric subjects off IS have no evidence of immune defect; they show robust T, B, and NK cell reconstitution, can be safely vaccinated and develop protective immunity. Transiently chimeric pts resumed endogenous hematopoiesis and were maintained on low-dose IS. There were two cases of GVHD: 1 subject exhibited grade 1-2 acute GI GVHD that responded to corticosteroids, followed by mild chronic GVHD. The second pt presented late and died of treatment resistant GI GVHD with CMV 11 months post-Tx. There have been three graft losses, related to infections in subjects on IS. There have been three subject deaths. Over all patient survival is 91.8% and death censored graft survival 94.1%. Tolerant FCR001 subjects have significantly better renal function than comparable KTx on SOC IS. Hypertension and hyperlipidemia is more common in SOC than tolerant FCR001 pts.

Conclusion: High levels of durable chimerism and tolerance with a low (5.5%) incidence of GVHD has been achieved in mismatched recipients of KTx. There are significant long term medical benefits to establishing tolerance in KTx recipients using the FCR001 approach.

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215.9

Achievement of Persistent Mixed Chimerism in Recipients of Matched and Mismatched Living Donor Kidney Transplants in a Tolerance Induction Protocol

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Purpose: The induction of tolerance to kidney transplants after development of specific unresponsiveness of recipient immune cells to donor alloantigens allows elimination of maintenance immunosuppressive (IS) drugs while preventing graft loss due to rejection. We have previously reported successful induction of mixed chimerism and tolerance in recipients of fully HLA-matched living donor kidney and hematopoietic cell (HCT) transplants. This work continues in HLA-mismatched transplants, wherein achieving persistent mixed chimerism is more challenging.

Methods: Living donors underwent hematopoietic stem cell mobilization and leukopheresis 6 weeks before kidney donation. The recipient conditioning regimen for the HCT consisted of 10 doses of total lymphoid irradiation (TLI) and 5 doses of anti-thymocyte globulin (ATG) following kidney transplant, with HCT on day 11. The HCT consisted of CD34+ hematopoietic progenitor cells and CD3+ cells. Twenty-nine patients received fully HLA-matched living donor transplants. Twenty-five patients received HLA-mismatched (1-haplotype matched) living donor transplants with an escalating dose of CD3+ cells to enhance HCT engraftment. Six patients recently received HLA-mismatched living donor transplants with substitution of a dose of total body irradiation (TBI) for the final dose of TLI.

Results: Of the 29 fully HLA-matched living donor transplants, complete IS drug withdrawal was achieved in 24, all of whom had at least 6 months of persistent mixed chimerism. Of the 24, 17 are alive, well and have been off IS drugs from 4 to 14 years without evidence of rejection. Two off IS drugs died due to cardiovascular events at 2 and 3 years. Two returned to IS drugs after loss of chimerism at 1 year followed by acute rejection at 4 years off IS drugs, and 3 after relapse of kidney disease at 1, 5 and 6 years off IS drugs. In the 25 1-haploype matched living donor transplants, mixed whole blood chimerism persisted in 10 (mean 20% chimerism) at the end of the 1st year posttransplant while immunosuppression was reduced to tacrolimus monotherapy. Chimerism was lost during the 2nd year in the 5 who were withdrawn from monotherapy; they returned to IS drug(s). Mixed chimerism without rejection has persisted in 3 maintained on IS monotherapy, for up to 5 years. The recent addition of a dose of TBI markedly increased levels and stability of mixed chimerism during the 1st year posttransplant.

Conclusions: The loss of chimerism during withdrawal of IS drug monotherapy in the HLA-mismatched transplants may have been due to the low level of whole blood chimerism, a contrast to the HLA-matched. A very low single dose of TBI added to the TLI/ATG conditioning regimen increased early chimerism. The stability of high levels of mixed chimerism after complete IS drug withdrawal during the 2nd year posttransplant is the subject of continuing investigation.

215.10

Tolerant Kidney Transplant Recipients Display a Unique CTLA-4 Dominant Urinary Cell mRNA Signature

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Introduction: Urinary cell mRNA profiling provides an unparalleled window into the intra-graft events in kidney transplant recipients. Utilizing this powerful molecular tool, we aimed to characterize mRNA signatures associated with human kidney allograft tolerance induced with tolerogenic CD6+ TCR-facilitating cells (FCR001) and a nonmyeloablative conditioning regimen.

Methods: We developed a custom panel of mRNAs encoding immunoregulatory proteins implicated in allograft tolerance and rejection and measured absolute levels of urinary cell mRNAs using preamplification enhanced real time quantitative PCR assays. We quantified urinary cell mRNA levels in 28 biopsy-matched urines from 14 FCR001-tolerant patients with durable chimerism and off immunosuppression (FCR Durable Cohort); 43 biopsy-matched urines from 34 kidney allograft recipients prospectively enrolled in the Clinical Trials in Organ Transplantation-04 (CTOT-04) and with biopsies with acute cellular rejection (TCMR Cohort); and 161 biopsy-matched urines from 124 kidney transplant recipients prospectively enrolled in CTOT-04 and with biopsies without rejection features (No Rejection Cohort).

Results: Urinary cell mRNA profile of the FCR Durable Cohort was unique and discriminated the tolerant patients from the patients with TCMR biopsies and the patients with No Rejection biopsies. Absolute levels of urinary cell mRNAs, summarized in Table 1, show that the median level of CTLA-4 mRNA is significantly higher in the FCR Durable Cohort (median 439 copies per microgram of RNA) than in the TCMR cohort (13S copies) or the No Rejection Cohort (13 copies) (KW P= 1x10-11). The differential gene expression pattern resulted in the ratio of CTLA-4 mRNA to granzyme B mRNA to be significantly higher in the FCR Durable Cohort (3304 copies) or the No Rejection Cohort (337 copies) (KW P= 1x10-11). The differential gene expression pattern resulted in the ratio of CTLA-4 mRNA to granulysin mRNA to be significantly higher in the FCR Durable Cohort (5.62 vs. 1.99,P=0.21).

Conclusion: Kidney allograft tolerance induced with CD6+ TCR-facilitating cells and a nonmyeloablative conditioning regimen is associated with a tolerogenic signature of enhanced expression of CTLA-4 mRNA and decreased expression of mRNA for granulysin B and perforin. The research was supported, in part, by NIH grants U01AI63589 and R37AI051652.
215.11

Evaluating Kidney Transplant Characteristics and Outcomes in Patients With Henoch-Schönlein Purpura

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Introduction: Henoch-Schönlein Purpura (HSP) is a small-vessel vasculitis characterized by deposits of immunoglobulin A (IgA) in target tissues. HSP is more frequently seen in children and usually has benign and self-limiting renal involvement; however, it is estimated that up to 2% of children with HSP nephritis can develop End-Stage Renal Disease (ESRD) and require renal replacement therapy. Due to the infrequency of HSP causing ESRD, large-scale studies of HSP and kidney transplant (KT) outcomes are scarce.

Methods: We used data from Scientific Registry of Transplant Recipients to evaluate differences for HSP patients listed for KT. Adult and pediatric patients listed from October 1987 to April 2021 were included. Recipients without HSP were randomly selected and matched in a 3:1 ratio to HSP recipients according to age (exact year), gender, ethnicity, donor source (living versus deceased), and year of transplantation (+3 years). Inferential statistics were used to evaluate differences between HSP and non-HSP patients. Regression modeling using a forward conditional approach and Kaplan-Meier survival analysis with a Mantel-Cox log-rank test were performed to calculate survivals and compare outcomes.

Results: During the study time period, 504,878 KT were performed; 893 (0.17%) were for HSP. Compared with non-HSP patients, HSP KT recipients were younger (30.6±14.2vs 47.2±15.8; p<0.001) and more commonly Caucasian (87.5% vs 68.6%; p<0.001), received a living donor allograft (44.5% vs 32.9%; p<0.001), and female (46.3% vs. 39.5%; p<0.001). Most HSP KT patients were preemptive (79.8%). A total of 773 HSP recipients were matched to 2,319 non-HSP recipients. For HSP patients, 1-, 3-, and 5-year death-censored graft survival (DCGS) was 87.3%, 70.4%, and 53.3%, respectively. For matched non-HSP patients, DCGS was 86.9%, 70.2%, and 52.5%, respectively (all p<0.05). Overall patient survival for HSP patients was 89.8%, 72.4%, and 56.6% at 1, 3, and 5 years, respectively. Overall patient survival for matched non-HSP patients was 89.3%, 72.9%, and 55.4% at 1, 3, and 5 years, respectively (all p<0.05). Acute rejection and graft thrombosis were the two leading causes of graft loss for both HSP (28.6% and 19.0%, resp.) and non-HSP patients (18.8% and 31.6%, resp.). In HSP patients who did not suffer recurrence, 1-, 3-, and 5-year DCGS was 95.8%, 88.8%, 81.3%, and 64.0%, respectively. Using regression model analysis of HSP KT patients for recurrence, older age (OR, 96% CI 1.05, 1.03-1.07, p<0.001) was significantly associated with recurrence; while a living donor allograft (OR, 0.50, 0.32-0.79, p=0.003) and a higher BMI (0.95, 0.91-0.99, p=0.020) were protective.

Conclusion: In a contemporary cohort of HSP KT patients, we demonstrate comparable graft and patient survival for HSP patients, compared to matched non-HSP patients, and superior survival if recurrence can be avoided.

215.12

Renal Handling of Phosphorus Very Early After Kidney Transplantation in Adults

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Introduction: To our knowledge there are no studies that describe phosphorus behavior in the early days of post kidney and simultaneous kidney-pancreas transplant. We aim to describe the urinary handling of phosphorus as well as the bone and mineral metabolism immediately before and during the first 8 days of post transplantation.

Methods: Observational descriptive longitudinal study including 61 renal and simultaneous kidney-pancreas transplant adult recipients (either living or deceased donors) at Hospital CEMIC Buenos Aires. Baseline blood samples were drawn pre transplant and then after surgery along with urine samples at days 1,3,5, and 7 to measure serum phosphorus, calcium, creatinine, pre-transplant intact parathormone (iPTH), urinary phosphorus and creatinine excretion, glomerular filtration rate (by urinary creatinine clearance), and fractional excretion of phosphorus.

Results: Mean age was 49 ± 13, 54% were male, 90% were kidney transplants, 75% received organs from deceased donors, average serum vitamin D was 22.1 ng/mL, 37% had hyperparathyroidism (iPTH>580 pg/mL) and 13% had hypoparathyroidism (iPTH<120 pg/mL) before transplant. We observed that creatininemia decreased (6.9 mg/dL at day 1 and 2.0 mg/dL at day 7 p=0.001) and also serum phosphorus decreased (6.2 ± 1.9 mg/dL at day 1 and 4.2 ± 2.8 mg/dL at day 7 p<0.001), while serum calcium and phosphaturia increased [0.5 g/day (0.1-1.3) at day 1 vs 0.63 g/day (0.4-0.88) at day 7 p<0.015] during the follow up. Interestingly, there were no changes in phosphorus fractional excretion (PEF) (table 1). In subgroup analysis recipients of living donors showed lower phosphatemia (4.8 mg/dL vs 6.7 mg/dL at day 1, p=0.000, and 2.2 mg/dL vs 4.8 mg/dL at day 7, p=0.000) probably related to the greater GFR and substantially higher phosphaturia [1.44 g/day (0.81-1.69) vs 0.29 (0.8-0.76) at day 1, p=0.000], on the other hand, PEF was lower when compared to deceased donors recipients (DOR). Among DOR (n=48), those without delayed graft function (n=29) (DGF) had higher GFR and phosphaturia during the whole study, [a greater phosphorus excretion was statistically significant at day 1 and 3: 0.54 g/day vs 0.10 g/day p=0.000 at day 1, 0.85 g/day vs 0.10 g/day at day 3, 0.77 g/day vs 0.47 g/day p=0.09 at day 5, 0.71 g/day vs 0.42 g/day p=0.07 at day 7 (table 2), and there was no difference regarding PEF compared to those with DGF. Patients were divided by tertiles of iPTH, and there were no differences in any measured aspect and also no correlation between iPTH and phosphaturia.

Conclusion: In this study we observed how phosphaturia improves with the recovery of GFR while PEF remains unchanged. This finding suggests that the tubules and interstitium, together with the hormonal context might not play a significant role in phosphorus handling at this point when the organ is still regaining function.
215.13

Outcomes for Septuagenarians Listed for Renal Transplant: A Good Option for Many

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Introduction: Kidney transplantation improve survival in the vast majority of patients with end-stage renal failure, but this is contentious in patients over 70 years old, for whom it is widely perceived that there is quality-of-life benefit but not an overall survival benefit. Since the change in national kidney matching scheme was introduced, more patients over 70 are receiving transplants and the potential benefits for this group are worth re-examination.

Methods: Data were collected from 117 patients aged over 70 at the time of acceptance for the deceased donor transplant waiting list and patient survival compared from date of listing between the transplanted group and non-transplanted groups using both Kaplan-Meier and competing risks methods.

Results: 1 year survival was 98% in the transplanted group compared to 92% in the non-transplanted group. 5 year survival however reported significant differences, with 75% survival in the transplanted group versus 37% survival in the non-transplanted group. In the 5-year competing risks analysis, we observed that the probability of being transplanted is more likely than the risk of death on the waiting. Transplant survival, including death with functioning graft was compared for three age groups (under 50, 50-70 and over 70), and was relatively similar in all groups until year 2, when uncensored transplant survival probability in the over 70s dropped relative to the other groups. At 5 years, there was a 45% transplant survival probability compared to 87% and 76% in the under 50 and 50-70 age groups respectively.

Conclusions: Selected patients over 70 at the time of listing achieve a survival benefit from transplantation. With better access to transplantation in the new kidney matching scheme, transplantation is expected to be a more realistic outcome for older patients on the waiting list and age alone should not be a barrier to acceptance.

215.14

Steroid Avoidance and Progression of Interstitial Fibrosis Assessed by Automated Quantification After Kidney Transplantation: A Multicenter Randomized Non-Inferiority trial (the ASTRONEF Study)

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Introduction: Corticosteroid avoidance has emerged as a standard of care in the low-immunological risk kidney transplant recipients as it does not increase the risk of acute rejection. However, another concern is the 1-year post-transplantation onset of interstitial fibrosis (IF) that could be mitigated by steroids. In that randomized clinical trial, we addressed whether the absence of corticosteroids impacted the progression of the fibrosis, assessed at implantation and at 1-year post-transplantation.

Methods: Adult recipients, of a renal allograft from a non–HLA-identical living or deceased donor were randomly assigned to receive on top of basiliximab, advagraf and MMF, steroid-free regimen (-CS group) or a standard corticosteroid tapering regimen (+CS group). Protocol biopsy was performed at implantation then at 3 and 12 months and interstitial fibrosis (IF) was assessed with a validated quantitative and automated method and expressed as a percentage. The primary endpoint was the difference in percentage change in IF between the implantation and the 1-year biopsy, with a hypothesis of non-inferiority of 10%.

Results: One hundred and eighty patients were analyzed in the full analysis set: 52 patients in the +CS group and 56 in the -CS one. Complete avoidance of corticosteroids was reached in 36 (64%) -CS patients that make up, along with all the 52 +CS patients, the per-protocol (PP) population. Figure 1 illustrates the distribution of the percentage of IF at each time points according to the treatment group. In the FAS population, mean percentage of IF at implantation was 19.5(±7.9)% in the -CS group (n=51) and 17.9(±7.3)% in the +CS group (n=49) (p = 0.3) and 25.9(±11.0)% (n=43) vs 21.5(±12.2)% (n=39) (p = 0.03) at 1-year. The progression of IF between the biopsy at implantation and at 1-year was of 7(±13.1)% (n=42) and 4.2(±11.5)% (n=37) in the -CS group and +CS group respectively (p = 0.3). When considering the difference, the steroid-free regimen was non-inferior 3.5% IC 95% [-0.5%; 7.5%]. In the PP population the progression of IF in the -CS group was of 4.2(±12.8)% and also steroid-free regimen was non-inferior (2.0% IC 95% [-2.7%; 6.7%]). By 1 year after transplantation, biopsy-proven acute rejection occurred in 4(7.1%) patients of -CS group versus 2(3.8%) of +CS group (p = 0.7).

Conclusion: In a randomized multicenter clinical trial, we found that steroid avoidance in kidney transplant recipients with low immunological risk, was non-inferior regarding the progression of interstitial fibrosis during the first-year post-transplantation assessed with a quantitative metric.

[Figure 1. Percentage of cortical interstitial Fibrosis assessed by automatic quantification on 1st implantation and protocol biopsies, according to the treatment group (Full Analysis Set population, n=274).]
Perioperative Changes in Glycemic Indices Using Continuous Glucose Monitoring in Kidney Transplantation Recipients

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Introduction: The plethora of data on glycemic excursions and additional indices, such as the glycemic variability (GV) and glucose management indicator (GMI), which is an estimated A1C derived from the glucose measures that the continuous glucose monitoring (CGM) system provides, has revolutionized the study of dysglycemia on various organs and stress induced situations. GV has been proposed to be a risk factor for complication of diabetes and increased mortality and predictive marker for hypoglycemia. The purpose of this study was to describe the changes in glycemic patterns of kidney transplant recipients during the perioperative period using CGM and attempt to define the clinical significance of the glycemic variability that occur.

Method: A prospective observational study starting May 1st, 2021 was conducted for patients who underwent kidney transplantations at our center. Upon enrollment, a CGM system was applied and CGM was undertaken 2 weeks preoperatively and 2 weeks postoperatively. No additional interventions were undertaken. Clinical characteristics and transplant related outcomes were collected along with glucose profile using the CGM system.

Results: By March 1, 2022, a total of 72 patients were enrolled in the study and completion of both preoperative and postoperative CGM was accomplished in 51 patients. A hyperglycemic tendency was seen postoperatively than preoperatively with higher mean glucose levels (110.49±38.65 mg/dL vs. 134.24±52.74 mg/dL; p<0.001), longer time above glucose level of 250mg/dL (3.13±9.19% vs. 4.24±8.118%; p=0.001), higher daily peak glucose levels (129.52±52.32 mg/dL vs. 160.58±42.47 mg/dL; p<0.001), higher daily nadir glucose levels (85.84±26.73 mg/dL vs. 105.27±27.83 mg/dL; p<0.001). The GV and GMI as measured by the CGM system were also significantly increased from preop to postop; 28.48±7.78% vs. 32.70±9.05%; p=0.004 and 5.91±0.92% vs 6.89±2.51%, p<0.001, respectively. Linear correlations fitted for postoperative glucose variability showed a positive correlation with preoperative glucose variability (r=0.40; p=0.006) and postoperative one-month hbA1c (r=0.35; p=0.023). A negative correlation with postoperative glucose variability and postoperative one-month fasting insulin (r=0.40; p=0.009), HOMA-B (r=-0.34; p=0.0029) and c-peptide (r=-0.49; p=0.001) was seen.

Conclusion: The continuous glucose monitoring of kidney transplantation recipients showed an overall hyperglycemic change in the post-transplant period with increased GV that was also reflected by an increase GMI and correlation with postoperative 1 month hbA1c. The negative correlations with postoperative GV and postoperative 1 month fasting insulin, c-peptide and HOMA-B values may relate to GV as a predictive marker of hypoglycemia, as reported in other studies. However, as an interim report of an ongoing prospective study, no conclusive statements about clinical significance could be made.
Survival Benefit of Deceased Donor Kidney Transplantation for Aboriginal and Torres Strait Islander Australians

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Aim: To quantify the survival benefit of kidney transplantation for Aboriginal and Torres Strait Islander Australians (respectfully referred to as Aboriginal Australians).

Background: Aboriginal Australians suffer a disproportionate burden of kidney failure. Community partnerships have consistently identified kidney transplantation as a priority for the Aboriginal community, yet rates of transplantation remain low. A perception of poorer transplant outcomes for Aboriginal Australians has been cited as a contributing factor to the inequity. This does not inform the best treatment options for Aboriginal Australians living with kidney failure.

Methods: Through analysis of the Australian and New Zealand Dialysis and Transplant (ANZDATA) registry we modelled the survival benefit of transplantation for adult Aboriginal Australians who commenced dialysis 1/07/06–31/12/19 and were subsequently included on the kidney-only, deceased donor transplant waitlist. Extended Cox regression models with transplantation included as a time-varying exposure compared overall patient survival of transplantation to remaining on dialysis.

Results: We identified 451 Aboriginal Australians who were waitlisted for kidney transplantation, 324 of whom received a deceased donor transplant. Transplantation conferred a significant survival benefit over remaining on dialysis after the first 12 months with a hazard ratio (HR) of 0.46 [0.23-0.93], p<0.05. This benefit was similar to that seen in the general waitlisted population; HR 0.49 [0.40-0.60], p<0.001; interaction p=0.24.

Conclusions: Deceased donor transplantation provides a survival benefit after 12 months for Aboriginal and Torres Strait Islander Australians. These data can provide confidence in waitlisting Aboriginal Australians who are otherwise eligible for transplantation. Efforts to improve equity in transplantation for Aboriginal Australians should be prioritised.

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QSant, a Multi-analyte Urine-based Test, Types the Injury of DGF and Its Recovery

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Introduction: QSant, a urine-based test quantitates alloimmune injury (AI) and acute rejection (AR) in the allograft via analysis of 6 biomarkers - cfDNA, methylated cfDNA, total protein, CXCL10, clusterin and creatinine. It utilizes a machine learning based algorithm for prognostication of injury and rejection risk. We propose the application of QSant to monitor Al in DGF and its recovery. Also use QSant as a surrogate to biopsy and refine the need for biopsy when the rejection risk is high.

Methods: 65 HLA-DR matched, renal allograft recipients, on TAC/MMF/prednisone, had 431 serial urine samples collected for QSant, over the 3 months post-transplant(MPT). All patients received a single 3mg/kg dose of antithymocyte globulin within 24 hours of graft re-vascularization. Clinical DGF was observed in 57% of the cohort. 62/65 (92%) of patients had a biopsy in the first month post-tx, with 80% of biopsies in the first week. Of the clinical DGF patients, 13% received a surveillance biopsy. Only 12% of biopsies had histological AR, others showed AI. QSant was used for quantification of AI (Q-Score >32) or immunequiescence (Q-Score <32) and a time-series analysis was performed. A PCA probed individual biomarker contributions in DGF patients to determine if specific biomarkers could predict recovery from IRI.

Results: The QSant biomarker profile for BPAR is significantly different from pure DGF without AR. A multivariate logistic regression of BPAR - with median Q-Score: 59(95% CI 50 – 69) - established cfDNA to be the most significant (p=0.029). QSant time-series analysis showed a significant (p=5.8e-19) decline from AI (Q-Score:47) to allograft stability (QScore:13) over the 3 MPT. The associated 30% decline in Q-Score indicative of allograft stability was also significant (p=8.66e-10). A significant decline (p=0.004) in rejection risk with Q-Score dropping into immunequiescence was observed after the first 2 weeks. In patients with recovery from DGF, concomitant with Q-Score there was a 3.6x (p=9.4e-6), 3x (p=1.42e-5) and 3x(p=0.00243) decline in clusterin, total protein and CXCL10, respectively. In the DGF sub-cohort that recovered function, PCA showed Clusterin explained 52% of the variance. For the samples with no histological evidence of rejection (n = 21), 90%(n=19) of the biopsies were done within the first two weeks post-transplantation. 36% of these had a Q-Score > 55: cases where QSant identified potentially evolving rejection missed by biopsy. 26% had Q-Scores in the immunequiescent range: samples where QSant might obviate the need for a biopsy.

Conclusions: Serial monitoring with QSant captures cases of DGF with concomitant AR and the early onset and resolution of DGF-related renal injury. QSant confirms recovery of allograft IRI in 90% of patients at 3 mo post-tx. Persistently elevated Q-Scores in a small subset of DGF patients suggests closer monitoring of these patients for increased risk of AR and chronic allograft injury over time.

Acute Tubular Injury and Necrosis Do Not Lead to Meaningful Elevations in Donor-Derived Cell-free DNA (dd-cfDNA)

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KOAR registry:

Introduction: Associations between non-rejection histologic diagnoses and dd-cfDNA have not been extensively characterized. We explored these associations in kidney transplant recipients enrolled in the Kidney allograft Outcomes AllSure Registry (KOAR, NCT03326076).

Methods: For-cause and surveillance biopsies with an event of acute tubular injury/necrosis, acute tubular injury/necrosis (ATI/ATN), and paired dd-cfDNA within 30 days were included. The incidence of a composite outcome (eGFR decline > 25%, rejection, and de novo donor-specific antibody detection) at 12 months after biopsy was also assessed.

Results: 166 biopsies (141 patients) with NR and 70 biopsies (64 patients) with ATI/ATN were included; compared to patients with ATI/ATN, patients with NRF had lower KDPI (49% vs 64%, p <0.05) and shorter cold ischemia time (13 vs 18 hours, p=0.01). ATI/ATN biopsies were more likely to be for-cause (81.4% vs 59.6%, p=0.001), earlier post-transplant (83.0 vs 116.5 days, p=0.001), and occur at lower eGFRs (43 vs 32 mL/min, p=0.001) (Table 1). There was no significant difference in median dd-cfDNA between NR (0.23%, IQR: 0.11 - 0.53) and ATI/ATN (0.21%, IQR: 0.13 - 0.55) biopsies (p = 0.993) (Figure 1). When patients were stratified by dd-cfDNA at the time of their first biopsy (p < 0.5% vs ≥ 0.5%), there was a non-significant trend towards a higher incidence of the 12-month clinical composite among those with dd-cfDNA ≥ 0.5% (27.5% vs 12.9%, p=0.53), with eGFR decline being most common (78.5% of events).

Conclusions: Our findings suggest that acute tubular injury/necrosis is not associated with substantial elevations in dd-cfDNA. The use of dd-cfDNA to identify patients with non-actionable histologic findings (including ATI/ATN) may allow more nuanced clinical decision-making and reduce the number of unnecessary biopsies.
Enhanced Histological Yield and Actionable Findings When Biopsy Is Guided by Donor-derived Cell-free DNA (dd-cfDNA)

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Introduction: Implementation of molecular biomarkers in kidney transplantation has expanded the amount of information available to clinicians before deciding to pursue biopsy. We evaluated how use of donor-derived cell-free DNA testing (dd-cfDNA) impacts histologic biopsy yield.

Methods: 1663 kidney transplant (KTx) recipients enrolled in the Kidney allograft Outcomes AlloSure Registry (KOAR, NCT03326076) were followed with dd-cfDNA post-transplant; testing was obtained either as part of a surveillance strategy or for-cause; indications for biopsy and histologic diagnoses were captured. This analysis included only for-cause biopsies.

Results: 65 biopsies (from 59 pts) driven by elevated dd-cfDNA levels were compared to 540 biopsies (392 pts) obtained for causes other than elevated dd-cfDNA. Patient age (55 vs 56 years), percent deceased donor (84.75% vs 78.83%), and biopsy timing post-transplant (123 vs 105.5 days) did not differ between groups (Table 1).

Among dd-cfDNA-guided biopsies, yield was enriched for rejection (48% vs 29%) and included fewer cases of ATI/ATN (12% vs 22%) compared to biopsies obtained for other causes (p<0.05) (Figure 1). Among dd-cfDNA-guided biopsies with rejection (ABMR, TCMR, or Mixed), median dd-cfDNA was 1.46% (IQR: 1.15 - 2.87). Among biopsies not performed due to elevated dd-cfDNA but with paired results available (n = 267), median dd-cfDNA was 0.24%. Within this group, patients with rejection had median dd-cfDNA of 0.82% and demonstrated an increase of 133% from the preceding result.

Conclusions: Dd-cfDNA surveillance enhances the histologic yield for actionable results in for-cause allograft biopsies. A low dd-cfDNA result can obviate the need for biopsy even in the presence of other clinical factors that are routinely used to guide the biopsy decision.
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Wide Spectrum of Molecular Injury Highlights Heterogeneity of Banff Tubulitis and Interstitial Inflammation Lesions

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Introduction: The pathological definition and clinical significance of borderline T cell-mediated rejection (BL-TCMR) remains an area of active debate, leading to inconsistencies in therapeutic strategy. Previously published data suggests that donor-derived cell-free DNA (dd-cfDNA) levels at the time of BL-TCMR diagnosis may identify patients at risk of adverse long-term outcomes. We characterized dd-cfDNA levels associated with BL-TCMR among patients enrolled in the Kidney allograft Outcomes AlloSure Registry (KOAR, NCT03326076).

Methods: Patients with BL-TCMR findings (Banff 2019) on either for-cause or surveillance biopsy and a dd-cfDNA result within 30 days were included in the analysis. Patients with biopsies showing isolated tubulitis or interstitial inflammation without tubulitis were also analyzed.

Results: We identified 56 cases of BL-TCMR with paired dd-cfDNA results (obtained within 30 days); median dd-cfDNA among these patients was 0.34% (IQR:0.17 - 1.00) (Figure 1a). The differences in dd-cfDNA among individual BL-TCMR combinations (t1/i1, t2/i1, t3/i1, t1/i2, t1/i3) were not significant, though the number of t3/i1 (n = 3, dd-cfDNA = 0.04%, 4.85%, 9.06%) and t1/i3 (n = 1, dd-cfDNA = 3.03%) cases was small. No differences were observed between biopsies with BL-TCMR and those with isolated tubulitis (t1/i0, t2/i0) or isolated inflammation without tubulitis (t0/i1) (Figure 1b). 31 of 56 BL-TCMR cases had prior dd-cfDNA measurement, with median result of 0.24% (IQR: 0.20 - 0.37) obtained 63 (IQR: 53.5 - 100) days before the index biopsy. The median percent increase between these sequential results was 55% (IQR: -9 - 235%).

Conclusions: Substantial heterogeneity is observed both with regards to dd-cfDNA levels at the time of BL-TCMR and the trajectory of dd-cfDNA preceding index biopsy. More importantly, no differences in dd-cfDNA are observed between BL-TCMR and t/i lesions not presently included in Banff criteria for BL-TCMR. These findings suggest that BL-TCMR, isolated tubulitis, and isolated inflammation without tubulitis represent a spectrum of molecular injury that may be further.
Beneficial Addition of Donor-derived Cell-free DNA Testing in Pediatric Kidney Transplantation

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Background: Donor-derived cell-free DNA (dd-cfDNA) is a useful plasma biomarker to assess allograft injury and rejection in kidney transplant recipients (KTRs). Serial monitoring of dd-cfDNA is recommended to monitor allograft rejection and to determine adequacy of immunosuppression. Although, serum creatinine increase is a marker for allograft dysfunction, it is limited by variations in hydration status, increased muscle mass, and growth in children. Herein, we describe a single-center experience on 1) the indications for performing dd-cfDNA fraction in pediatric KTRs and 2) comparison of dd-cfDNA fraction in various clinical states.

Methods: This is a cross-sectional observational single-center study in pediatric KTRs who were tested for dd-cfDNA in plasma for a clinical indication. Children were categorized according to the indication for testing and the median values of dd-cfDNA were noted for each category. Comparisons were made by Kruskal Wallis test between each category. P < 0.05 was considered significant. Receiver Operating Characteristic (ROC) curve analysis was performed to analyze the sensitivity and specificity of dd-cfDNA to predict biopsy-proven graft injury.

Results: dd-cfDNA was performed in 77 children transplanted at the Miami Transplant Institute with a mean age of 11.6 ± 5.9 years; 54 (70%) were male. Seven (9%) were second transplants. Mean time from transplant to time of dd-cfDNA testing was 3.5 ± 3.2 years (range 1 month to 19 years). Indications for testing included highly sensitized state or development of alloantibodies (N=12), clinical suspicion of rejection (N=7), BK nephropathy (N=1), low immunosuppression because of leukopenia, viral replication or recurrent bacterial infections (N=30), fluctuating serum creatinine (N=7), increased serum creatinine with normal growth (N=6), increased post-transplant baseline creatinine for age (N=10) and non-adherence (as evidenced by low tacrolimus levels without change in kidney function; N=4). There was a significant difference in dd-cfDNA between children who had biopsy-proven acute rejection (BPAR) rejection, BK virus nephropathy (BKVN) and those who had alloantibodies (median 1.35 (95% CI 0.6,2.4) versus those who did not [median score: 0.3 (95%CI 0.25, 0.45); Figure 1]. ROC curve analysis revealed high specificity and sensitivity for dd-cfDNA to predict graft injury and presence of alloantibodies (Figure 2).

Conclusions: dd-cfDNA is a clinically useful adjuvant tool to determine allograft injury in pediatric kidney transplant recipients. Traditionally, immunosuppressive drug levels have been used to determine immunosuppression dosing. dd-cfDNA helps distinguish immune activation versus immune quiescence and has the potential to guide and serially monitor immunosuppression dosing.

[Graph showing indications for dd-cfDNA testing and ROC curve analysis]

*In multiple comparisons, there is a significant difference between BPAR and alloantibodies from categories with low ISP change in ISP and increased baseline creatinine.
Regulatory T Cell Biomarkers Identify Patients at Risk of Developing Acute Cellular Rejection in the First Year Following Heart Transplantation

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Background: Acute cellular rejection (ACR), an alloimmune response involving CD4+ and CD8+ T cells, is a leading cause of mortality and morbidity following heart transplantation. While immunosuppressive drugs such as corticosteroids and calcineurin inhibitors (e.g., cyclosporine, tacrolimus) have largely reduced ACR events immediately following transplantation, ACR remains a risk factor in the long-term, with outcomes including graft loss and death. The balance between a conventional versus regulatory CD4+ T cell alloimmune response is believed to play a major role in the development of ACR. Therefore tracking these cells following transplantation would elucidate if changes in these cell populations could signal ACR risk. Understanding this link could be an important step towards developing tools that can detect and/or prevent ACR.

Methods: To describe changes in conventional versus regulatory CD4+ T cells during the course of heart transplantation, we used a CD4+ T cell gene signature panel (TGS) that tracks CD4+ T conventional (Tconv) and regulatory cells (Treg) on longitudinal samples from 94 adult heart transplant recipients. We investigated Tconv and Treg levels pre-transplant vs. post-transplant, as well as between non-rejection and ACR samples. Also, we compared TGS with HEARTBiT assay, a gene expression assay for exclusionary diagnosis of ACR in heart transplant patients in the first year following transplantation, on ACR diagnosis performance while also investigating its prognostic utility.

Results: Compared to pre-transplant samples, non-rejection samples showed increased Treg- and decreased Tconv-gene expression while such differences were reduced in ACR samples. Within the post-transplant samples, we saw that the TGS panel could discriminate between ACR and non-rejection samples with comparable performance to the HEARTBiT assay. When HEARTBiT and TGS were combined, they showed improved specificity to HEARTBiT alone (up to 10% increase in specificity at the same sensitivity level). Furthermore, within the first two months following transplantation, Treg genes showed reduced expression in patients who had developed one or more ACR events. Reduced Treg gene expression was positively associated with younger recipient age and higher intra-patient tacrolimus variability.

Conclusion: We demonstrated that expression of genes associated with CD4+ Tconv and Tregs could identify patients at greater risk of ACR. Also, complementing HEARTBiT with TGS improved the diagnostic performance of HEARTBiT. Taken together, these biomarker tools may have clinical utility in heart transplant care.

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Dynamic Kidney Graft Failure Risk Prediction Using Serial Donor Derived Cell Free DNA

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Background: Donor-derived cell free DNA (ddcfDNA) has evolved as a non-invasive biomarker for monitoring kidney transplant patients for rejection. Trends in ddcfDNA over time may help predict important outcomes for the allograft. We examined samples from subjects enrolled in the CTOT08 clinical trial (NCT01289717) to determine the ability of joint modeling to dynamically predict graft survival in kidney transplant recipients.

Methods: Serial blood samples collected in the first two years post-transplant were analyzed for ddcfDNA using the TRAC test (Eurofins – Viracor, Lees Summit, MO). We used joint modeling method to model the trend of serial ddcfDNA score to predict the 5-year death censored graft survival. We pre-defined 6 time points post-transplant and dynamically plotted two patients 5-year graft survival via the joint modeling method.

Results: Figures of predicted graft survival probability of two illustrative patient examples are presented below. Both patients have high 5-year graft survival probability based on their serial ddcfDNA scores up to 0.3-years post-transplant. Moving forward in time and follow up, the predicted probabilities start to diverge for these two patients. At the 2-year time point, for patient 1 with stable serial ddcfDNA scores, the predicted 5-year graft survival probability is 0.968 with 95% CI [0.918, 0.990]. For the other patient (2) whose ddcfDNA scores continue to increase over time, the predicted 5-year graft survival probability is 0.770 with 95% CI [0.404, 0.959]. The second patient had a graft failure at 4.88 years post-transplant.

Discussion: Plasma ddcfDNA is evolving as both a diagnostic and a prognostic biomarker in the management of kidney transplant recipients. Using joint modeling, we were able to develop a dynamic risk prediction model for graft failure in patients. Future applications include further validation and eventually defined interventions to reduce the risk of graft loss.
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Urinary Extracellular Vesicle DNA Cargo Reflects Kidney Allograft Injury

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Introduction: Following allograft injury, donor-derived cell-free DNA (dd-cfDNA) levels increase. Numerous research studies have demonstrated increased dd-cfDNA levels in blood and urine as biomarkers of kidney allograft injury in patients with transplanted kidney. Extracellular vesicles (EVs) are nanosized particles released by almost all cells. Because of the anatomical proximity of kidney EV-producing cells and urine, (dd)DNA containing urinary EVs (uEVs) are potentially relevant biomarkers of allograft injury. The aim of our study was to explore uEVs and their DNA cargo, to reveal their association with allograft injury and finally to compare their biomarker potential with (dd)cfDNA found directly in the urine of patients with transplanted kidney.

Method: We collected a second morning urine sample from 40 patients before surveillance or for-cause biopsy. We also collected blood and biopsy samples for donor-recipient genotyping. Considering histological analysis, we divided patients into normal histology, rejection injury (combination of antibody- (ABMR) and T-cell mediated rejection (TCMR)), and non-rejection injury group. First, we isolated uEVs (using protocol based on size-exclusion chromatography), their DNA cargo (uEV-DNA), and cfDNA from urine. We used nanoparticle tracking analysis to determine the concentration and size of uEVs. For DNA parameter analysis, including yield, copy number, integrity index, and donor-derived fraction, we used fluorometry and digital droplet PCR. We applied DNase assay and electron microscopy (TEM) immunogold labelling technique to investigate whether DNA was present inside or outside the uEVs.

Results: The median uEV concentration was 8.47x10¹⁰/ mmol U-creatinine. The concentration was similar in all patient groups, whereas the size parameter differed significantly, as patients with rejection and non-rejection injury had significantly larger uEVs compared with patients with normal histology (177.5 nm and 174.1 nm vs. 160.7 nm, respectively; P=0.045). DNA co-isolated with uEVs and in several parameters correlated with urinary cfDNA. For uEV-DNA, the copy number of donor-derived DNA was significantly higher in patients with ABMR than in patients with TCMR (3044.3 vs. 680.9 copies, respectively; P=0.036). Regarding the long/short gene amplicon ratio, uEV-DNA (green) was less fragmented compared with cfDNA (yellow; Figure 1C). The TEM DNA labelling showed that the DNA was bound to the EV surface. uEV-DNA characteristics correlated with interstitial inflammation, inflammation in areas of fibrosis, and combination of glomerulitis and peritubular capillaritis Banff scores.

Conclusion: In kidney transplant recipients, DNA bound to the surface of uEVs reflects allograft injury, particularly allograft rejection and is therefore a suitable potential biomarker for kidney allograft injury.
Higher Urinary Mitochondrial DNA Level From COVID19 Recovered Renal Allograft Recipient Patients Induces Inflammatory Cytokine Secretion in Peripheral Blood Mononuclear Cell

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Introduction: Severe acute respiratory corona virus-2 (SARS-CoV-2) affected multiple organs including the Kidney. SARS-CoV-2 open reading frame protein 3a induces necroptosis in the infected cell leading the release of death-associated molecular pattern (DAMPs) ligands like mt-DNA, which binds to TLR9 and trigger innate immunity may lead to acute allograft injury.

Material and Methods: Sixty-six (n=66) live-related renal allograft recipients previously hospitalized with SARS-CoV-2 infection were recruited after 2-3 weeks of discharge. Patients were categorized in either non-AKI (n=47) or acute kidney injury (n=19) group if hospitalization serum creatinine level was >30% of pre-Covid serum creatinine. A 50ml urine sample was collected for the mitochondria gene NADH-ubiquinone oxidoreductase chain 1 (ND-1) and nuclear 36B4 gene quantification and urine N-GAL measurement by the RT-PCR and ELISA. A 10ml blood sample from 10 healthy volunteers was collected for PBMCs isolation. Urinary DNA from all AKI patients was pooled together and 1x10⁶ PBMCs were stimulated for 24 hrs. with 1 µg/ml of urinary DNA or CpG oligodeoxynucleotide(d5'-tcgtcgttttccggcgc:cgcgccg-3') in duplicate in 6 well culture plate. The gene expression of cytokines IL-10, IL-6, MYD88 was analyzed by the RT-PCR and supernatant cytokines IL-6 and IL-10 level was measured by the ELISA.

Results: The pre-covid creatinine in non-AKI vs AKI patient was 1.06±0.20 vs 0.97±0.27, p=0.14, at hospitalization was 1.27 ± 0.18 vs 1.84 ± 0.37, p=0.001, at discharge was 1.09±0.20 vs 1.11±0.32 mg/dl, p=0.73. The mean ND-1 gene Ct in AKI group was (19.44±2.58 a.u) compared to non-AKI (21.77±3.60; p=0.013). The normalized ND-1 Ct in AKI was (0.79±0.11 a.u) compared to non-AKI (0.89 ± 0.14; P=0.007). The median urinary N-GAL level in AKI group was (453.53; range, 320.22-725.02, 95% CI) ng/ml com-pared to non-AKI (212.78; range, 219.80-383.06, 95%CI; p=0.015). The median urine creatinine normalized uNGAL was 4.78 (0.58-70.39) ng/mg in non-AKI group compared to 11.26 ng/mg (0.41-329.71) in AKI group. The area under curve of ND-1 gene Ct was 0.725, normalized ND-1 Ct was 0.713 and uNGAL was 0.663 and normalized uNGAL was 0.667 for detecting the mitochondrial stress in patients who had AKI (Figure.1A-D). The IL-10 gene expression was downregulated in umt-DNA treated PBMCs compared to control (-3.5±0.40 vs 1.02±0.02, p<0.001). IL-6 gene expres-sion was upregulated (3.65±0.42 vs 1.06±0.02, p<0.001). Myd88 expression was upregulated (2.45±0.31 vs 1.04±0.02, p=0.015). The culture superna-tant IL-10 level was lower in umt-DNA treatment PBMCs compared to control (10.65±2.02 vs 30.3±5.47, p=0.001). The IL-6 level was (200.2±33.67 vs 47.6±12.83, p=0.001) (Figure.2 A-E).

Conclusions: Renal allograft of post-COVID-19 recovered patients experiences mitochondrial distress. Quantification of mt-DNA can detect the post covid mitochondrial distress with higher sensitivity compared to uNGAL. umt-DNA induces a robust inflammatory response in PBMCs may exacerbate the allograft dysfunction. Brijesh Yadav, acknowledge the Young Scientist Research Grant (Grant No YSS/2020/000202/PR CYSS) support of the Department of Health Research, New Delhi, India.
Pretransplant Micrornas in Liver Per fusate Associate With Early Allograft Dysfunction

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Introduction: Early allograft dysfunction (EAD) in liver transplantation (LT) is associated with poor long-term graft and patient survival. Prior to LT, while organs are stored or reperfused, they release uniquely packed EVs in response to ischemic conditions. Capturing the spill of EV-derived miRNAs into perfusate will allow for a better understanding of the early stress signals that culminate in EAD. To date, there are no established molecular biomarkers used in clinical decision-making in transplantation.

Methods: Per fusate was collected from 24 LT patients. EVs were quantified using TRPS and Imaging Flow Cytometry. Total RNA was isolated using the miRNAeasy Micro Kit (Cat # 74004). MiRNA expression was evaluated using Human miFinder miScript miRNA PCR arrays (MIHS-1162) which include 84 of the most abundantly expressed miRNAs and 12 control wells. To identify the differentially expressed miRNAs, ΔΔCt values were calculated by performing global normalization of each plate. In silico prediction of miRNA targets was done using the top 100 genes from miRDB and gene lists were analyzed using Metascape. EAD was defined by the presence of i) total bilirubin ≥ 10mg/dL or INR ≥ 1.6 on day 7, and/or ii) ALT or AST > 2,000 IU/L within the first 7 days.

Results: Using 600μl of perfusate, we recovered an average of 1.5x10^8 EVs (images in Fig 1A). Three miRNAs (miR-1260a, miR-4454, miR-5100) were found to be overexpressed (p<0.05, FC≥2; Fig 1B) in the perfusate of LT patients who experienced EAD (n=4) compared to those grafts which functioned normally (n=20). MiRNAs were associated with metabolic processes and DNA repair (Table 1). Interestingly, the MELD score, a validated predictor of survival in patients with cirrhosis, was significantly lower in the EAD patients (p=0.006), showing an opposite trend than expected. No other donor/recipient characteristics were statistically significant between groups.

Conclusion: The presence of donor-specific EVs in perfusate evidences the capacity for these structures to facilitate intercellular and interorgan communication prior to LT. Per fusate miRNAs were also found to function as specific, noninvasive biomarkers assessing risk of EAD, even in the absence of significant clinical characteristics. Such findings further elucidate the pretransplant biological responses that influence LT outcomes, and may ultimately guide posttransplant management.

<table>
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<td>Metabolism of lipids, regulation of response to DNA damage stimulus, chromatin organization</td>
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Spatial Protein Profiling of Leukocyte Infiltrates in Renal Biopsies After Cellular Therapy

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Background: Regulatory T cells (Tregs) are powerful modulators of immune function, and are of increasing interest as an adoptive cellular therapy for the treatment of transplant rejection. Elucidate the impact of Treg therapeutics in vivo is crucial to identify the therapeutic efficacy. This study aimed to examine the infiltrated leukocytes to provide a clearer picture of the dynamic process that occurs in the transplanted tissue after cellular therapy compared to rejection.

Methods: Cellular infiltrates were assessed by GeoMx digital spatial profiling (DSP) platform in tissue biopsies from three transplant patients who received Treg therapy and two control patients with confirmed rejection, with biopsies taken at similar time points after transplantation (6-12 months). Various regions of interest (ROIs) were selected (9 -12 regions) from each patient with diverse infiltration types (Figure 1). In addition, FOXP3hi CD4+ and FOXP3low/neg CD4+ regions were selected from both groups to assess the protein signatures of these cellular infiltrates.

Results: The FOXP3 signal was highly enriched in regions from cell therapy patients compared with rejection ROIs that in rejection ROIs, suggesting a link between infused Tregs and allograft infiltration by B cells. Conversely, the rejection ROIs have a high expression of Ki67, indicating the presence of highly proliferative cells. The monocyte/macrophage markers CD14, CD68, and CD163 were also enriched in the rejection ROIs suggesting that macrophages may be associated with graft rejection in these patients. Further analysis revealed interesting differences between the cellular infiltrates in FOXP3hi segments from cell therapy patients compared with rejection group such as enrichment in proteins related to signalling, including STAT3 and p-STAT3, and coinciding with enrichment in regulatory molecules, including CTLA-4 and PD-1. VISTA protein was found to be highly enriched in FOXP3hi segments from cell therapy patients compared with rejection group such as enrichment in Treg-associated markers. Nevertheless, these Tregs failed to control the alleloimmune response. Our analysis suggests that FOXP3hi cells that are present in regions collected from rejecting patients may suppressive Tregs, since FOXP3hi cells coincide with enrichment of Tregs-associated markers. Nevertheless, these Tregs failed to control the alloimmune response, as demonstrated by the enrichment of CD8 T cells, which were notably represented in FOXP3hi regions in rejection tissues.

Conclusion: The GeoMx DSP allowed for an in-depth analysis of leukocyte infiltrates and provided comprehensive information about the molecular processes associated with stable renal allograft in patients receiving Treg therapy, which in turn may assist in understanding the mechanisms of therapeutic immune regulation and optimal timing for immunosuppression minimisation.
Validating a Cut-off of IgG Hypogammaglobulinemia as a Risk Factor of Severe Infection in Solid Organ Transplantation

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Background and aims: Severe infection is a leading cause of morbidity and mortality in solid organ transplantation. IgG hypogammaglobulinemia has been previously investigated in single and multicenter studies in distinct solid organ transplantations as a predictor of infection. We aimed to validate the IgG cut-off of 600 mg/dL as a risk factor of severe infection in solid organ transplantation. The potential utility of this biomarker is that this can be modulated by therapeutic intervention.

Materials and Methods: 538 heart, liver or kidney recipients were analysed in a prospective study performed in 2 centers. During a follow-up during the first 6 months after solid organ transplantation 298 (55.4%) patients developed at least one episode of severe infection the majority of which were bacterial infections. As a secondary outcome we retrospectively analysed the impact of IgG hypogammaglobulinemia early after transplantation on the rate of death. Survival analysis was performed by Kaplan-Meier. Risk for development of severe infection was also performed by logistic regression analysis.

Results: The rate of decrease of IgG after transplantation was similar in both participating centers. Cumulative survival without severe infection during the first 6 months after transplantation was lower in solid organ transplantation recipients with IgG hypogammaglobulinemia defined as IgG < 600 mg/dL at days 7 or 30 after transplantation (Log Rank 5.22, p=0.022). IgG hypogammaglobulinemia was associated with higher rates of death after solid organ transplantation (Log Rank 5.75, p=0.017). In logistic regression analysis IgG hypogammaglobulinemia was significantly associated with risk of severe infection (OR 1.635, p=0.040, 95%CI 1.022-2.615). IgG hypogammaglobulinemia was associated with higher rates of death after solid organ transplantation (Log Rank 5.75, p=0.017). In logistic regression analysis IgG hypogammaglobulinemia was significantly associated with risk of severe infection (OR 1.635, p=0.040, 95%CI 1.022-2.615). IgG hypogammaglobulinemia was a risk factor of death (OR 1.078; p= 0.011, 95%CI 1.190 – 3.668). We performed an immunological score for development of severe infection composed of pre transplant monocytes < 7% (2 points), IgG hypogammaglobulinemia (2 points), CD4 <400 cells/μL at day 30 (2 points), C3 <60 mg/dL at day 30 (2 points) and CRP >3 mg/dL at day 30 (2 points). In those patients with 4 or more points, OR for development of infection was 2.89 (95% CI 1.641 – 5.123; p<0.001).

Conclusion: IgG hypogammaglobulinemia (defined as IgG < 600 mg/dL early after transplantation) is associated with risk of severe infection in solid organ transplantation. This cut-off should be taken into account in future clinical trials that evaluate the impact of the modification of this risk factor by adding intravenous immunoglobulin to these patients to prevent severe infection. An immunological score combining IgG hypogammaglobulinemia and other innate and acquired immunity parameters could be a better way to identify the risk for development of severe infection in solid organ recipients.

Natural History of CXCR5+ Follicular-like Helper (TFH) Cells in Kidney Transplant Recipients With Rejection

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Introduction: TFH-like helper cells (Tfh) have been associated with donor-specific antibody (DSA) and antibody-mediated rejection (ABMR) in kidney transplant recipients. However, changes in Tfh according to rejection type are less clear. We sought to describe the natural history of Tfh by rejection type.

Methods: A pilot study of 4 recipients with ABMR were age-sex matched to recipients with TCMR, and recipients with no rejection. Prospectively collected blood samples were analysed retrospectively by cytometry by time of flight and manually gated to identify CD3+CD4+CXCR5+ Tfh (Figure 1). Pre-transplant Tfh frequency of CD3+ T cells was compared between rejection groups, pre-transplant DSA and de-novo DSA using student’s T-test. Change in Tfh frequency post-transplant was tested between rejection groups using linear mixed regression.

Results: Pre-transplant Tfh frequency was highly variable between individuals (median=3.3%, IQR=1.1-5.9) and not significantly different between rejection groups (p=0.7), those with and without pre-transplant DSA (p=0.4) or those that developed and did not develop de-novo DSA (p=0.7). Early post-transplant Tfh frequency decreased in recipients with subsequent TCMR or stable function but increased in those who developed ABMR (Figure 2). Of the four recipients with AMBR, three had a Tfh frequency increase within 60 days prior to ABMR. Change in Tfh frequency over time was 2.7% (95%CI=0.3-5.2) higher in ABMR than stable recipients, adjusting for pre-transplant DSA and de-novo DSA (p<0.001). There was no difference in the change of Tfh frequency between TCMR and stable recipients.

Conclusion: In the early post-transplant period and immediately before rejection, Tfh frequency increased above pre-transplant levels in patients who subsequently developed ABMR. This was not observed in stable patients or those with TCMR. These results will inform timepoints appropriate for screening in larger cohort studies.
The Association Between Regulatory T Cell Subpopulations and Severe Pneumonia Post Renal Transplantation

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Severe pneumonia accounts for the majority of morbidity and mortality in renal allograft recipients due to immunosuppressant maintenance. Regulatory T cells (Tregs), which are involved in tackling infections under immunosuppressive conditions, are rarely uncovered. We aimed to investigate the relationship between various Treg subpopulations and severe pneumonia after kidney transplantation (KTx). KTx recipients with pneumonia were divided into severe pneumonia (SP) and mild pneumonia (MP) groups. The frequencies and absolute numbers (Ab No.) of total Tregs (CD4+CD25+FoxP3+), six subsets of Tregs (Helios+/-, CD39+/-, and CD45RA+/-), and T cells, B cells, and NK cells were assessed from peripheral blood via flow cytometry using the t or Mann-Whitney test and receiver operating curve analysis. We also determined the median fluorescence intensity (MFI) of human leukocyte antigen (HLA)-DR on monocytes and CD64 on neutrophils. Logistic regression was used to identify the risk factors of disease progression and Pearson’s correlation analysis was performed to identify relationships between the measured immune indices and patients’ clinical information. Our research indicated that Treg subpopulations were strongly associated with severe pneumonia progression post KTx. Based on the monitoring of Treg subpopulations, better individualized prevention and therapy might be achieved for patients with severe pneumonia post KTx.

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**216.17**

**Multiplex Digital PCR for the Detection of Donor-derived Cell-free DNA**

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**Introduction:** Graft damage and failure are major problems after solid-organ transplantation. Biomarkers for monitoring transplanted patients provide new opportunities to substantially improve patient management, graft lifespan, and patient survival. There is strong evidence that donor-derived cell-free DNA (DD-cfDNA) increases when transplanted organs are damaged. The majority of this information is derived from tests using next-generation sequencing. Here we present an evaluation of new technology, multiplex digital PCR (mdPCR), which has the potential to revolutionize DD-cfDNA testing.

**Method:** This mdPCR method takes advantage of Luminex’s DigiMAP multiplex PCR chemistry and the QuantStudio Absolute Q Digital PCR platform (Thermo Fisher Scientific, previously Combinat). The bench work for mdPCR is completed in less than five hours. Data is analyzed using a custom R package. Assay performance characteristics were determined using artificial mixtures of genomic DNA, and inter-laboratory reproducibility was assessed.

Blood was collected from kidney and heart transplant recipients, cf-DNA was isolated using a variety of methods, and mdPCR was used to quantify DD-cfDNA levels.

**Results:** This methodology distinguished donor and recipient DNA and provided absolute quantification of the number of DNA copies. The following performance characteristics were determined: sensitivity, the limit of detection, and linear range, inter- and intra-assay consistency. Several factors affected performance including: DNA characteristics, probe design, primer design, and PCR reaction components. Results showed that high levels of DD-cfDNA are consistent with clinical observations and that rapid testing is feasible (< five hours).

**Conclusion:** The mdPCR approach has high promise to revolutionize diagnostic testing in cancer, infectious disease, and transplant monitoring. Our study demonstrates the advantages of this technology for the detection of DD-cfDNA which includes absolute quantitation, sensitivity, ease of use, short turn-around-time, and a relatively low cost when compared to next-generation sequencing techniques. A test with these features could transform the management of transplant recipients and lead to prolonged graft and patient survival.

**217.1**

**European Multicentre Heart Transplant Study Investigating the Effectiveness and Safety of Extracorporeal Photopheresis in a Real-world Setting**

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**Introduction:** Extracorporeal photopheresis (ECP) is recommended as an adjunctive therapy in prevention and treatment of acute cellular rejection (ACR) after heart transplantation (HTx) by a number of different clinical societies. However, these recommendations are based on studies conducted over 15 years ago. In clinical practice, ECP is also used to treat antibiotic-mediated rejection (AMR), to prevent rejection in patients at high risk of transplant rejection, or to reduce immunosuppression. The aim of this study was to describe the real-world use of ECP in the modern era of HTx and to assess the effectiveness and safety of ECP.

**Method:** Seven transplant centres located in five European countries participated in this retrospective, explorative, single-arm chart review study. Heart transplant patients who started ECP in 2015 or later were included in the study and were followed from HTx up to two years after the last ECP treatment. Data have been extracted from the medical charts covering patient characteristics, reasons for ECP treatment, schedule and duration of ECP treatment, concomitant immunosuppressive medication, clinical outcomes (e.g., graft function, rejections, and survival) as well as treatment-related complications and safety.

**Results:** Overall, 105 heart transplant patients treated with ECP were enrolled. Mean age of patients was 48 years and 70% were male. The main reasons to start ECP were ACR (n=37, 35%), AMR (n=16, 15%), mixed rejection (n=19, 18%), and prevention of rejection (n=33, 31%). Median time from HTx to start of ECP was 359 days. At time of analysis, 58 patients (55%) had completed ECP and in 47 patients (45%), treatment was ongoing. On average, 37 ECP treatments per patient were performed over a mean duration of 13 months. In 97% of patients who completed ECP, graft function was stable at the end of ECP (measured mainly by echocardiography). Of the 72 patients in the rejection groups, 31 had a biopsy at start of ECP and at the end of study period and 27 (87%) showed an improvement of ISHLT classification of ACR or AMR. In the prevention of rejection group, 27 of the 33 patients (82%) remained free from any rejection after starting ECP despite patients considered as being at high risk of rejection or having reduced immunosuppression. For 57% (n=33) of patients who completed ECP (n=58), the main reason for stopping was positive response to treatment. Overall survival among the included 105 patients was 95% over a mean follow-up of two years from start of ECP. Five patients died, three with a functioning graft. No deaths were related to ECP. In total, 18 patients (17%) had an ECP-related safety event, of which 13 patients (12%) experienced complications with venous access.

**Conclusion:** The results of this largest European ECP study in HTx indicate that ECP is a safe and effective treatment not only for ACR but is also an option for AMR, mixed rejection, and prevention of rejection.
A Multi-institutional Study of Factors Determining Cardiac Allograft Function in Children at 3 Years Post-transplant: Absence of Impact of Donor Specific Antibodies

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Introduction: We previously showed that highly sensitized and non-sensitized pediatric heart transplant (PHTx) recipients had similar 1 year survival (CTOTC-04 study). In this follow-up study (CTOTC-09), we assess risk factors for impaired allograft function at 3 years post-Tx including the impact of ‘preformed’ (at Tx) and first year newly detected donor specific antibodies (ndDSA).

Methods: Consecutive children listed for Tx at 9 North American centers were prospectively enrolled. Management of sensitization, immunosuppression and rejection surveillance were standardized. The primary endpoint was pulmonary capillary wedge pressure (PCWP) at 3 years post-PHTx. Secondary endpoints included other hemodynamics measures, ejection fraction (EF), brain natriuretic peptide (BNP), graft and patient survival and rejection. DSA was defined as single antigen Luminex testing as ≥1 antibody specific to donor HLA antigens with MFI>1000 (based on core laboratory).

Results: Of 407 children enrolled, 370 achieved PHTx (mean age 8.7 years). Sensitization status at PHTx was as follows: non-sensitized (n=163, 44%), sensitized/no DSA (n= 115, 31%), sensitized/DSA+ (n=87, 24%); unknown (n=5 (1%) unknown. Baseline characteristics among these groups differed significantly by ethnicity (p=0.024), height (p=0.017), weight (p=0.017), ICU admission (p=0.009), and prior sensitizing events (p=0.027). At 3 years, subjects with vs. without early DSA (preformed and/or first year ndDSA) had comparable PCWP, EF, and BNP levels (Figure). There were also no significant differences between the 2 groups for other hemodynamic measures (pulmonary artery, right atrial, and left and right ventricular end diastolic pressures, cardiac index, EF, and BNP level (all P >0.05). For the 3 sensitization status groups at Tx, the presence/absence of first year ndDSA also did not influence any of these endpoints. Freedom from death or retransplant was not influenced by sensitization status at Tx, though freedom from rejection with hemodynamic compromise was inferior in those with one or more DSA at Tx >4000 MFI. Freedom from acute antibody mediated rejection was lowest in the non-sensitized group (p<0.001). Multivariable analyses showed that higher PCWP at 3 years post-Tx was associated with 3-year age (p=0.024), height (p=0.017), weight (p=0.017), and or prior sensitizing events (p=0.027). At 3 years, subjects with vs. without early DSA (preformed and/or first year ndDSA) had comparable PCWP, EF, and BNP levels (Figure). There were also no significant differences between the 2 groups for other hemodynamic measures (pulmonary artery, right atrial, and left and right ventricular end diastolic pressures, cardiac index, EF, and BNP level (all P >0.05). For the 3 sensitization status groups at Tx, the presence/absence of first year ndDSA also did not influence any of these endpoints. Freedom from death or retransplant was not influenced by sensitization status at Tx, though freedom from rejection with hemodynamic compromise was inferior in those with one or more DSA at Tx >4000 MFI. Freedom from acute antibody mediated rejection was lowest in the non-sensitized group (p<0.001). Multivariable analyses showed that higher PCWP at 3 years post-Tx was associated with 3-year age (p=0.017), height (p=0.001) and coronary artery disease (CAD, p=0.033) but not with DSA status (preformed and/or first year ndDSA). Adverse graft function was associated with weight (Odds Ratio (OR) 1.03; 95% confidence interval (CI) 1.02, 1.05; p<0.001); and any rejection with hemodynamic compromise (OR 7.91; 95% CI 1.37, 45.75; p=0.021) but not with DSA status.

Conclusion: Sensitization status at PHTx and development of first year ndDSA are not associated with worse allograft function or inferior survival at 3 years. Ongoing follow-up, including assessment of CAD, continues. This information is critical for defining transplant strategies and the long-term impact of DSA on graft outcomes.
Differences in Short-term and Medium-term Prognosis Between Female and Male Heart Transplant Recipients: Analysis of More Than 20 Years in a Single Center in Argentina

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Introduction: There are differences in the clinical course of advanced heart failure between men and women. In addition, it has been reported that the prognosis after heart transplantation may differ according to the gender of the recipient, with different results in the literature. The objective of this study is to characterize the demographic and clinical differences between male and female recipients in our population, as well as to analyze their short- and medium-term outcomes.

Method: Heart transplant recipients between February 1993 and February 2016 were retrospectively evaluated. Those with a follow-up of less than 5 years were excluded. Male and female recipients were compared and differences in short- and medium-term prognosis were analyzed. Quantitative variables are expressed as mean +/- standard deviation or median and interquartile range 25-75 according to their Gaussian distribution, and categorical variables as percentages. T-test or Mann-Whitney test was used to compare quantitative variables according to their normal distribution, and Fisher’s test to compare nominal variables. Survival at 5 years was analyzed using the log-rank test and plotted using Kaplan-Meier. Univariate analysis was performed and variables with a p<0.2 were used for multivariate analysis using Cox regression. A p<0.05 was considered significant.

Results: Overall, 489 patients were included, 369 men (75.5%) and 120 women (24.5%). The characteristics of the population are shown in Figure 1A. The median age was 52 years (IQR 41-59), with the women being younger and with a lower body mass index (BMI). Regarding the etiology, idiopathic cardiomyopathy was more frequent in women and ischemic cardiomyopathy in men. There were no differences in elective status, level of hemodynamic support, or pre-transplant ischemia times. Although the women received donors with lower BMI, the size mismatch was greater in this group at the expense of oversize. The incidence of primary graft dysfunction (PGD), severe PGD, and in-hospital mortality was similar between men and women, however, female recipients had higher 5-year mortality (34.4% vs. 45% OR 1.56; CI 1.03-2.37; p=0.039), without differences in the causes of death (Figures 1B and 2). In the multivariate analysis, female recipient, PGD and emergency condition were independent predictors of 5-year mortality. When analyzing the subgroup of female recipients, PGD and size mismatch at the expense of oversize were associated with higher mortality, however, in the multivariate analysis, only PGD maintained statistical significance. (HR 2.45, CI 1.19-4.26, p= 0.013) (Figure 3).

Conclusion: Female heart transplant recipients have a worse prognosis in the medium term with higher mortality at 5 years, without differences in hospital mortality. Larger studies are required to elucidate the underlying mechanisms with their potential therapeutic implications.
217.4
A New Allocation System for Priorization in Heart Transplantation in the State of São Paulo - Brazil: Its Impact on Patients in ECMO

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Objectives: VA ECMO has become one important tool to treat patients with chronic cardiomyopathy who are on waiting list for heart transplantation (HT) and acutely worsens and need mechanical support. Some studies showed worse results, but with changes in the allocation system, these patients are designated to higher status, which can impact the outcomes. Our allocation system was modified in 2021. The objective of our study was to analyze the impact of the new allocation system on the results of patients bridged to HT using VA ECMO in a high volume heart transplant center.

Methods: Of the 298 HT performed between 2016 and 2021 in our center, 125 (42%) were in use of inotropic support, 150 (50%) were bridged with intra-aortic balloon pump and 23 (8%) patients were bridged with VA ECMO. 20 patients were also in ECMO support, but died on waiting list. About 75% of patients bridged with ECMO were during the last 3 years.

Results: Our mean list mortality on ECMO before the new allocation system (2016-2020) was 61.8% and after the new allocation (2021), 28.5%. The mean waiting time on ECMO was 7.2 days with the old system and 4 days after the new system. The survival to hospital discharge was 55% for patients bridged with ECMO in the old system and 80% for patients in the new allocation system. The total operative mortality during the old allocation system was 13.06% and 5.26% in the new allocation system.

Conclusions: The new allocation system positively influenced the mortality of patients bridged with VA ECMO to HT. The waiting list mortality was reduced, the days on ECMO were reduced and the survival to hospital discharge was improved.

217.5
Renal Failure in Patients Bridged to Lung Transplant With ECMO: Risk Factors and Outcomes

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Introduction: Extracorporeal membrane oxygenation (ECMO) is a well-established intervention as a bridge to lung transplantation (BTT) in critically ill patients with excellent outcomes. However, some patients deteriorate despite ECMO support, developing multiorgan failure including acute kidney injury (AKI), which often requires continuous renal replacement therapy (CRRT). While the majority of AKI-on-ECMO patients are no longer considered candidates for transplant, the outcomes of those patients who are transplanted despite AKI-on-ECMO are poorly understood. Therefore, this study examined risk factors for development of AKI-on-ECMO prior to transplant as well as the long-term renal outcomes in patients successfully transplanted with AKI-on-ECMO.

Methods: We retrospectively identified 84 patients who were supported on ECMO with the intent to BTT at our institution between 2010-2020. Outcomes of those who developed AKI-on-ECMO BTT were compared with those without AKI-on-ECMO BTT, as well as to those that developed AKI on ECMO but were not transplanted (failed BTT). χ² test for independence for categorical variables and Student’s t-test for continuous variables were used. Renal function was examined for the first 3 years post-transplant in the patients transplanted with AKI to evaluate renal recovery.

Results: Forty-seven patients were successfully bridged to transplant, with 6 (12.8%) developing an AKI pre-transplant while on ECMO (2 of the 6 required CRRT pre-transplant). Patients with AKI had different lung pathologies (p=0.006), were more likely to be on central ECMO (p=0.002) compared to those without AKI-on-ECMO BTT and had longer post-transplant hospital stay (p=0.015). Of the 39 patients who failed BTT, 14 (35.9%) developed AKI. Compared to patients successfully transplanted with AKI, the failed BTT were shorter (p=0.045) and received more transfusions while on ECMO (p=0.035). All 6 patients with AKI-on-ECMO BTT required CRRT post-transplant for between 1 and 18 days; 4 patients were transitioned to intermittent hemodialysis (iHD) prior to discharge. Long-term, 2 patients had near-complete renal recovery within 2 months following transplant, 2 patients transitioned off iHD but without return of renal function to pre-transplant baseline, and the remaining 2 continued iHD. Five patients were alive 3 years post-transplant, with 1 death due to metastatic malignancy. At 3 years, mean peak post-transplant FEV1 %−predicted was 77.6 and no significant rejection events had occurred.

Conclusion: This study evaluated renal outcomes in patients who developed acute kidney injury while on ECMO as a bridge to lung transplantation. More than half of the patients did not require iHD within months, with the two youngest returning to their baseline creatinine. Our results suggest that AKI while on ECMO bridge may not represent an absolute contraindication to transplantation and in carefully selected patients can lead to optimal long-term outcomes.
ECMO as a Bridge to Lung Transplantation for COVID-19 ARDS Patients at Houston Methodist Hospital

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Introduction: During the pandemic, the use of ECMO support and bridging to lung transplant increase substantially in severe COVID-19 adult respiratory distress syndrome (ARDS) patients. We report thirteen cases from our institute in which the patients were treated with veno-venous (VV) ECMO for severe ARDS from COVID-19 infection and successfully received bilateral lung transplant in 2021.

Method: A total of 71 lung transplants were performed at our institution in 2021, including 17 lung transplants for severe COVID-19 ARDS. 13 of these 17 patients were cannulated for VV ECMO, either VV-ECMO plus mechanical ventilation, or VV-ECMO only. Demographics, clinical characteristics and outcome were analyzed.

Results: All patients were male with median age 42 years (24-60 years). The median BMI of the recipients was 26 (21-34). The median lung allocation score (LAS) was 90 (89-95). 6 patients had no prior remarkable past medical history, 7 patients had known comorbidities including hypertension, type II diabetes mellitus, chronic kidney disease and/or chronic heart failure. None of patients had underlying lung disease. Eleven recipients received bilateral lung transplants and two recipients received bilateral lung transplant plus a kidney transplant. The median bridging time on ECMO was 91 days with a range of 49 to 170 days. Femoral-femoral VV ECMO cannulation was initiated urgently in most patients. Once the patients were stabilized, the VV ECMO configuration was converted to Protek Duo (n=8), Avalon (n=2), or Crescent cannula (n=2) and one patient continued on femoral-jugular VV ECMO (Figure 1). At the time of transplant, 2 patients were supported with mechanical ventilation via tracheostomy in addition to ECMO, 6 patients had tracheostomy in addition to ECMO, 5 patients were on ECMO only. Total 11 patients were “awake ECMO”, all participated physical therapy (7 patients ambulated daily). Pre-transplant, the average hospital length of stay (LOS) was 64 days (9-141), the average ICU LOS was 17 days (7-47). The total LOS was 91 days (43-122). Complications during ECMO treatment included gastrointestinal bleeding, septic shock, acute kidney injury, right ventricular failure, pneumothorax. Post-transplant complications, such as AKI, RV dysfunction, pericardial effusion, dysphagia, gastroparesis, appear to have similar incidence as in non COVID-19 lung transplant population. 12 patients were decannulated from ECMO during the transplant procedure, one patient was re-cannulated for VV-ECMO due to aspiration and decannulated after three days. 4 patients discharged home, 8 patients were transferred to rehabilitation facilities. One patient died 7 months post-transplant with pneumonia, sepsis and multi-organ failure.

Conclusion: The prolonged VV-ECMO support is feasible for highly selected patients who are eligible to be bridged to lung transplantation. Awake VV-ECMO and prehabilitation are good prognostic indicators for patients who can benefit from lung transplant.
Neutrophil Extracellular Traps Removal Using Ex Vivo Lung Perfusion Restored Lung Function in Gastric Aspiration Damaged Porcine Lungs

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Background: Lung transplantation (LTx) is an established therapeutic option for end-stage pulmonary disease. However, it remains hampered by donor lung scarcity. Treatments which could regenerate lungs rejected for transplant should be explored in order to combat waiting list mortality. Aspiration induced acute lung injury (ALI) is one of the contributes to the low utilization of donor lungs. Neutrophil extracellular traps (NETs) are implicated in the inflammation profile of ALI. Reduction of NETs could be used as a therapeutic option with the arrival of devices specific to their removal. NucleoCapture device selectively removes NETs from the blood by utilizing human histone H1.3 protein conjugated to polymer beads. This study investigated the impact of the NETs capture device during ex vivo lung perfusion (EVLP) on ALI damaged lungs.

Methods: Healthy pigs (n=12) were stratified into two groups, treated (n=6) and not treated (n=6). All animals received 4ml/kg body weight gastric content distributed equally between the different lung segments using a bronchoscopy to induce acute lung injury. Mild to moderate ARDS was developed over 6 hours and confirmed via blood gas values, chest x-ray imaging and histological examination. Lungs were subsequently explanted en bloc and placed on EVLP for 4 hours. Treated lungs were placed in line with a NucleoCapture device connected to the EVLP circuit and the non-treated group underwent the same EVLP protocol without the device.

Results: Aspiration induced ALI was induced in all subjects as confirmed by infiltration on chest x-ray, histopathological examination and by PaO2/FiO2 ratio. Following treatment with the NucleoCapture device during 4 hours of EVLP, the PaO2/FiO2 ratio was significantly increased compared to non-treated lungs and was found to surpass the threshold values suitable for transplantation. Furthermore, macroscopic evaluation of the treated lungs demonstrated improvement relative to both the initial injury as well as comparison with the non-treated cohort.

Conclusions: Removal of NETs using the NucleoCapture device did restored lung function in aspiration damaged lungs. The amelioration of lung function by removing NETs shows potential clinical use of the device to increase the donor lung pool for lung transplantation.

How to Do It: Use of Octopus Tissue Stabilizer for Minimal Manipulation Approach of the Bronchial Anastomosis in Lung Transplant

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Introduction: Bronchial anastomotic complications (BAC) are a cause of grave concern for surgeons that perform lung transplantation. There are several risk factors that may lead to this complication, being inadequate surgical technique one of them, specifically regarding the adequate exposure and manipulation of the bronchial stump and anastomosis.

Method: We report the use of the Octopus Tissue Stabilizer (Medtronic, Inc, Minneapolis, MN) as a mean of allowing for a better exposure of the stump and facilitate a “no touch” approach towards the anastomosis.

Results: The Octopus Tissue Stabilizer (Medtronic, Inc, Minneapolis, MN) is a validated device for cardiac surgery as a tissue stabilizer for off-pump coronary artery bypass. It utilizes vacuum at the extremity of its “U” shaped claw to soothe the beating of the heart on a designated spot and assist the cardiac surgeon. Our idea was to employ the distal claw of such device to stabilize the bronchial stump and perform the bronchial anastomosis with a “no touch” technique. As we did not have a need to smooth the beating of the heart, the suction mechanism was kept turned off (FIGURE 1). It is important to report that in this case, as in others, several other techniques were applied to reduce BAC (the use of end-to-end anastomosis and pericardial flap), therefore it is impossible to affirm that the application of the Octopus Tissue Stabilizer (Medtronic, Inc, Minneapolis, MN) is responsible for the favorable outcome of this patient.

Conclusion: We believe that the systematic application of devices that facilitate the employment of the correct surgical techniques can have an effect in reducing the incidence of BAC, while providing no additional risk to the patient.
Activation of Angiotensin-converting Enzyme 2 (ACE2) Modulates Lung Mechanics in a Brain Death Model and Attenuates Pulmonary Edema After Rat Lung Transplantation

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Introduction: Lung transplantation is a therapeutic option established worldwide for end-stage lung diseases. However, as most donors evolve with brain death (BD), the donated lung may have been compromised. In view of the participation of the renin angiotensin system (RAS) and the use of angiotensin-converting enzyme 2 (ACE2) activators in several pathological processes, it was investigated how diminazene aceturate (DIZE), an ACE2 activator, modulates hemodynamic and blood gas changes, as well as lung function following transplantation in rats.

Method: Male Lewis rats were randomly distributed in the following experimental groups: intact, brain death (BD) and BD + diminazene aceturate (BD+DIZE). The last two groups were submitted to brain death process, treated with saline (0.9%) or DIZE (15 mg/kg-1) and kept on mechanical ventilation for 6 hours (donor). After this period, cardiopulmonary block extraction and left unilateral transplantation (LTx) with independent graft ventilation was performed, followed by 2h reperfusion. Hemodynamics (mean arterial pressure - MAP), blood gas analysis, lung mechanics, and pulmonary edema were evaluated. Results are presented as S.E.M. (ANOVA; Tukey; p<0.05). (Approval # CEUA/FMUSP - 1630/2021).

Results: The administration of DIZE, 3 hours after BD, prevented the increase in the MAP (210' after BD-induction: BD – 110 ± 12 mmHg; n=5; BD+DIZE – 40 ± 12 mmHg; n=4/ p=0.0001) without associated blood gas and metabolic alterations. Changes in lung mechanics, such as decreased tissue damping (G) and histeresivity (n) followed by increased respiratory system compliance (Crs), were associated with BD+DIZE (G - 0,25 ± 0,03 cmH2O/mL; Crs – 0,71 ± 0,03 mL/cmH2O; n – 0,14 ± 0,008) compared to intact (G - 0,40 ± 0,02 cmH2O/mL, p = 0,01; Crs – 0,64 ± 0,01 mL/ cmH2O, p = 0,02; n - 0,26 ± 0,01, p = 0,004) and BD groups (G – 0,41± 0,05 cmH2O/mL, p = 0,02; Crs – 0,61 ± 0,01 mL/cmH2O, p = 0,01; n - 0,25 ± 0,008, p = 0,01) (Figure 1). After LTx, MAP, gas exchange function, and lung mechanical parameters, were not different among the 3 groups (p>0.05). On the other hand, the DIZE treatment was capable to reduce wet-to-dry weight ratio (INTACT – 1,87 ± 0,13; BD – 2,59 ± 0,14; BD+DIZE – 1,93 ± 0,15/ p=0,01) (Figure 2).

Conclusion: Our data suggests that activation of ACE2 is able to modulate donor hemodynamic and lung mechanical parameters, probably reducing tissue resistance and improving airflow in the peripheral airways, converging to a decrease in ventilation heterogeneity in the sudden onset model of brain death. Our data also indicates that DIZE attenuates pulmonary edema on grafts from BD donors after lung transplantation.

Keywords: Diminazene aceturate. Renin-angiotensin system. Brain death. Lung mechanics. Lung transplantation.
230.1

Incidence and Severity of COVID-19 Infections Among Triple-vaccinated Solid Organ Transplant Recipients During the Omicron Variant Surge in the United States (12/25/2021-3/1/2022)

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Introduction: Incidence and severity of SARS-CoV-2 Omicron variant infections among vaccinated solid organ transplant recipients (SOTRs) is unknown. We surveyed SOTRs from our national observational cohort (United States) during the Omicron wave (12/25/2021-3/1/2022).

Methods: 1467 triple-vaccinated SOTRs who reported no prior positive COVID-19 test were surveyed regarding new COVID-19 infections after 12/25/2021. A subgroup underwent serologic testing for anti-spike antibodies between 11/26/2021 and 3/7/2022 on two clinical assays (Roche Elecsys anti-receptor binding domain [RBD] assay or Euroimmun anti-S1 assay). If SOTRs reported a new COVID-19 infection, the most recent pre-infection antibody result was used. Otherwise, the preceding antibody level closest to 12/25/2021 was used.

Results: 1467/1801 eligible SOTRs responded to the survey (81.6%) and 666 underwent serologic testing. 175/1467 (12%) reported suspected or test-confirmed COVID-19 infection during the Omicron wave; 150/175 (86%) reported having a positive PCR or home COVID-19 test (Omicron-confirmed). SOTRs who were Omicron-confirmed were younger (median [IQR] 55 [44-67] vs. 62 [50-68], p<0.001) and more likely to be using azathioprine (11% vs. 6%, p=0.009) (Table 1). Regarding illness severity, 11/164 (7%) reported hospital admission for COVID-19, 59/173 (34%) reported high-fevers or dyspnea, 93/173 (54%) reported mild cold-like symptoms, and 9/5 (5%) were asymptomatic. Symptoms included nasal congestion (71%), cough (61%), malaise (58%), headache (57%) and sore throat (57%) (Table 3A). Two SOTRs died during the study period; family members reported that these deaths were secondary to COVID-19 infection. Among the 666 SOTRs who underwent serologic testing, 46/666 (7%) were Omicron-suspected or confirmed; 37/46 (80%) tested positive via PCR or home test. The 46 Omicron-suspected or confirmed were more likely to be lung transplant recipients (20% vs. 8%, p=0.008), with greater number of immunosuppression medications (median, [IQR] 3 [2-3] vs. 2 [2-3], p=0.03), including tacrolimus (91% vs. 77%, p=0.02), steroids (72% vs. 59%, p=0.008), and calcineurin inhibitors (80% vs. 86%, p=0.02). 39/46 reported symptom duration of median (IQR) 7 (4-10) days, 4/37 reported hospital admission, and 1/4 to an intensive care unit (Table 3B). 37/46 (80%) of Omicron-suspected or confirmed and 534/620 (86%) of no-Omicron (p=0.002) were positive for anti-spike antibodies before the Omicron wave. 50% of Omicron-suspected or confirmed and 72% of no-Omicron SOTRs had anti-RBD anti-RBD>250 U/mL or anti-S1>4 AU (p=0.002)(Table 2).

Conclusion: Test-confirmed COVID-19 infections were reported in 5.7% of vaccinated SOTRs during the Omicron wave. COVID-19 infection appeared correlated with lower pre-Omicron wave antibody levels. These findings highlight the importance of layered prevention strategies for the immunocompromised including social distancing, masking, vaccination and passive immunity strategies. This work was supported by the Ben-Dov family, the Trokhin Patterson family, grants T32DK007713 (Dr. Alejo), K01DK101677 (Dr. Massie), and K23DK115908 (Dr. Garonzik-Wang) from the National Institute of Diabetes and Digestive and Kidney Diseases; grant K24AI144954 (Dr. Segev) from the National Institute of Allergy and Infectious Diseases; and grants U01AI138897 and K23AI157893 (Dr. Werbel).
Protective Effect of HLA-A24 Allele on COVID-19 Among Vaccinated Kidney Transplant Recipients

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Introduction: Human Leukocyte Antigen (HLA) alleles have been shown to affect both the susceptibility and severity of viral infections. [1] Recently, seasonal coronavirus-specific CD8+ T cells were found to cross-react with HLA-A24 high binding epitope from SARS-COV2 spike protein in healthy persons with HLA A-24 alleles. [2] Considering that HLA-A24 antigen has been found in high frequency in Asian countries that have experienced the lowest death per capita, HLA-A24 allele may confer protection against COVID-19. Therefore, in this study, we examined the association of HLA-A24 allele and COVID19 susceptibility and severity in kidney transplant recipients (KTR).

Methods: A single-center cross-sectional study included 530 patients who received a kidney transplant between 2/1/2017 to 1/31/2022. The exposure was HLA-A24 allele and primary outcomes were COVID19 infection and COVID-19-related hospitalization or COVID-19-associated death. All positive COVID-19 KTR were either self-reported or were from PCR tests indicated for patients with COVID-19 symptoms. For further analysis, patients were stratified by vaccination status prior to COVID-19 infection. Data was analyzed using student’s T test, Chi square test, and Fisher exact test.

Results: Of the 509 KTR, 139 (27%) patients had at least one HLA-A24 antigen of which 13 patients were double-positive for HLA-A24. There were no significant differences in age, gender, race, ethnicity, BMI, and prevalence of comorbidities including coronary artery disease, diabetes, and heart failure between patients with and without HLA-A24 allele. Of 139 KTR with HLA-A24 alleles, 35 patients became infected with COVID-19; while 139 of 370 KTR without HLA-A24 had COVID-19 (25.2% vs. 37.5%; P <0.01). After stratified by vaccination status prior to COVID-19 infection, while the ratio of KTR with COVID-19 prior to vaccination did not differ between the two groups (20.1% vs. 22.4%, P =0.58), the proportion of patients who had COVID-19 after vaccination was significantly lower in the HLA-A24 group (5.0% vs. 15.1%; P <0.01). There was no difference in hospitalization and mortality related to COVID-19 between the two groups.

Conclusion: COVID-19 vaccination is more effective in KTR with HLA-A24 allele. Further studies are required to elucidate the mechanism of protective effect of HLA-A24 on COVID-19 in high-risk immunocompromised host such as in KTR.

References:
Antibody Response to a Third Dose of SARS-CoV-2 Vaccine in Heart and Lung Transplant Recipients

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Introduction: Heart transplant (HT) and lung transplant (LT) recipients have impaired humoral responses to SARS-CoV-2 vaccination that may be augmented after a third vaccine (D3). It is not known whether HT/LT recipients achieve high levels of anti-spike binding antibody required to neutralize the Omicron variant, and how long this endures after D3.

Methods: A total of 111 HT and 75 LT recipients without prior SARS-CoV-2 infection underwent anti-spike antibody testing with two clinical assays (Roche Elecsys anti-receptor binding domain (RBD) Ig [anti-RBD] and/or Euromimmun Ig [anti-S1] before, 1-, and 3-months after receiving D3 (BNT162b2, mRNA-1273, or Ad26.COV2.S). Population factors and antibody responses were compared using Fisher’s exact testing for categorical variables and Wilcoxon rank-sum testing for continuous variables.

Results: HT and LT recipients were similar with respect to age, sex, and time since transplant (Table). More LT recipients reported triple-immunosuppression (14% vs 71%, p<0.001). Before D3, 35/111(32%) of HT vs 42/75(56%) of LT recipients were negative for anti-spike antibodies. By 1 month post-D3, 24/35(69%) HT and 15/42(36%) LT recipients seroconverted (negative to positive antibody). This was approximately stable at 3 months post-D3; 24/35(69%) HT vs 16/39(41%) LT recipients. HT recipients had higher median anti-RBD and anti-S1 antibodies before D3, 1 month, and 3 months post-D3 on both assays at all timepoints (Figure 1A, 1B).

Conclusion: Although many HT recipients develop high-titer antibody response to a third dose of SARS-CoV-2 vaccine, LT recipients demonstrate low seroconversion rates and lower titers, reflecting heavier immunosuppression and suggesting higher COVID-19 risk. Strategies to augment vaccine immunogenicity including additional doses, mixing of platforms, and targeted immunosuppressive reduction may be indicated.

This work was supported by the Ben-Dov family, the Trokhan Patterson family, grants T32DK007713 (Dr. Alejo), K01DK101677 (Dr. Massie), and K23DK115908 (Dr. Garonzik-Wang) from the National Institute of Diabetes and Digestive and Kidney Diseases; grant K24AI144954 (Dr. Segev) from the National Institute of Allergy and Infectious Diseases; and grants U01AI138897 and K23AI157893 (Dr. Werbel).

Hailey Hardgrave1, Allison Wells2,3, Joseph Nigh2, Sushma Bhusal4, Mary K Rude5, Lyle Burdine3, Emmaouil Giorgakis3.
1College of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR, United States; 2Department of Surgery, University of Arkansas for Medical Sciences, Little Rock, AR, United States; 3Division of Solid Organ Transplantation, University of Arkansas for Medical Sciences, Little Rock, AR, United States; 4Division of Nephrology, University of Arkansas for Medical Sciences, Little Rock, AR, United States; 5Division of Hepatology, University of Arkansas for Medical Sciences, Little Rock, AR, United States.

Introduction: Vaccination against COVID-19 has been shown to reduce COVID-19 hospitalization and mortality rates in the general population. Studies in the Solid Organ Transplant (SOT) population report reduced COVID-19 mortality in vaccinated SOT recipients despite concerns over the effect of immunosuppression on vaccine response. Aim of this study was to perform a single center propensity score matching analysis on post COVID-19 survival of consecutive vaccinated and unvaccinated SOT patients who contracted the disease, at a single US academic transplant center.

Method: Study period was 02.2020-02.2022. After obtaining institutional IRB approval, all consecutive COVID-19 positive cases on adult SOT (liver, kidney or simultaneous liver-kidney) recipients were identified and registered on a constructed institutional REDCAP database. Variables captured included patient demographics, comorbidities, immunosuppression, COVID-19 treatment and hospitalization status, COVID-19 vaccination status, and 60-day mortality. Propensity score matching was performed on age and gender for completed vaccination status at time of infection. Multivariable and survival analysis were constructed from this matched data.

Results: 144 SOT patients were diagnosed with COVID-19. 98 were unvaccinated and 46 vaccinated. Mortality in unmatched data was 11.2% (N=10) and 2.2% (N=1) in unvaccinated and vaccinated groups respectively (table 1.1). Propensity score matching with adjustment reduced the study population to N=101. Multi-variant analysis for 60-day mortality for matched data identified age (OR 1.22, P<0.001) and post-kidney transplant status (OR 40.93, P=0.001) to significantly increase 60-day mortality odds (table 1.2), contrary to female gender (OR 0.13, p=0.005) and monoclonal antibody treatment (OR 0.06, p=0.014). Matched data Kaplan-Meier survival curve showed lower post-infection survival in the unvaccinated group (30 days; vaccinated vs. unvaccinated 97.8% vs. 89.1%, respectively) (60 days; 97.8% vs. 83.6%, respectively) (p=0.019) (figure 1). Majority of deaths for both vaccinated and unvaccinated groups occurred between 0 and 30 days (N=7 unvaccinated, N=1 vaccinated).

Discussion: In agreement with previously published reports, advancing age and post-kidney transplant status significantly impacted COVID-19 mortality, while monoclonal antibody treatment significantly decreased mortality, irrespective of vaccination status. Post COVID-19 matched data survival analysis demonstrated inferior survival in the unvaccinated group. Despite the limited sample size, this propensity score matching study supports the protective effect of COVID-19 vaccination on SOT recipients.
### Antibody Response and Molecular Graft Surveillance in Kidney Transplant Recipients Following SARS-CoV-2 Vaccination

**Nicolle Ali, Zoe Stewert, Jake Miles, Sapna Mehta, Vasiishta Tatapudi, Bonnie Lonze, Elaina Weldon, Charles Dimaggio, Jeanette Leonardi, Robert Montgomery, Herati Ramin.**

1Transplant Institute, NYU Langone Health, New York, NY, United States; 2CareDx, CareDx, Brisbane, CA, United States.

**Introduction:** Preliminary studies suggest that kidney transplant recipients (KTRs) show diminished humoral responses to SARS-CoV-2 vaccination. Although reports of allograft rejection around the time of SARS-CoV-2 vaccination have been rare, there is no recommended framework for monitoring for potential vaccine-related allograft injury. Here, we describe an approach for longitudinal assessment of immunogenicity and safety of SARS-CoV-2 vaccination in KTRs.

**Methods:** KTRs eligible for SARS-CoV-2 vaccination were identified through medical records, beginning March 12, 2021. Baseline and weekly blood samples were collected for routine assessment, SARS-CoV-2 spike protein antibody titers, dd-cfDNA (AlloSure, CareDx) and gene expression profiling (GEP) (AlloMap, CareDx) for 12 weeks. HLA DSA testing was performed at baseline, 2 weeks after completion of vaccine doses and at week 12. Antibody response was defined as a 10-fold increase in total binding IgG titer.

**Results:** 49 KTRs were identified for analysis. Patient demographics are summarized in Table 1. 10 patients (20%) demonstrated a spike antibody response following completion of the vaccine series. Patients with a prior history of COVID-19 were more likely to mount a spike antibody response (n=8, 53.3%) compared to those with no reported history of COVID-19 (n=2, 5.8%). The odds ratio was 18.3 (95% CI 3.2, 105.0, p=0.0006). Median dd-cfDNA levels did not differ between pre- and post-vaccination (0.23% versus 0.21% respectively; Table 2). There was no significant difference between baseline and post-vaccination GEP scores (9.85 versus 10.4 respectively; Table 2). No patients developed clinically significant DSA, eGFR decline or allograft rejection following vaccination.

**Conclusions:** Quantitative antibody responses were strongly associated with a diagnosis of prior SARS-CoV-2 infection. Stability of eGFR, dd-cfDNA, GEP profiles and lack of allosensitization reinforce the safety profile of SARS-CoV-2 vaccination in KTRs. Further studies are needed to better understand GEP profiles and lack of allosensitization reinforce the safety profile of SARS-CoV-2 vaccination in KTRs.

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### Ad.26.COV2.S Versus BNT162b2 or mRNA-1273 as a Third Dose in Solid Organ Transplant Recipients Seronegative After 2-dose mRNA Vaccination


1Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, United States; 2Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, United States; 3Department of Acute and Chronic Care, Johns Hopkins University School of Nursing, Baltimore, MD, United States; 4Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, United States; 5Department of Molecular Microbiology and Immunology, Johns Hopkins University School of Public Health, Baltimore, MD, United States; 6Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, United States; 7Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, United States.

**Introduction:** Heterologous vaccination (“mixing platforms”) for the third (D3) dose of SARS-CoV-2 vaccine is a potential strategy to improve antibody responses in solid organ transplant recipients (SOTRs), but data are mixed as to whether this provides any differential immunogenicity benefit.

**Method:** We assessed for differences in immunogenicity and tolerability of homogeneous (BNT162b2 or mRNA-1273; D3-mRNA) versus heterologous (Ad.26.COV2.S; D3-JJ) D3 among 377 SARS-CoV-2 infection naive SOTRs who were seronegative after two mRNA vaccines. We measured anti-spike titers and used weighted (age and organ type) Poisson regression to evaluate prevalence of seroconversion and development of high-titers, comparing D3-JJ to D3-mRNA, at 1, 3, and 6-months post-D3. Titers measured after a fourth dose of vaccine, receipt of monoclonal antibodies, or SARS-CoV-2 infection were excluded from analyses.

**Results:** 40 D3-JJ recipients and 337 D3-mRNA recipients were similar in sex, years since transplant, and mycophenolate use. At 1-month post-D3, 63% of D3-JJ recipients and 52% of D3-mRNA recipients became seropositive (p=0.28); this difference did not reach statistical significance in weighted analysis (weighted incidence-rate-ratio wIRR=2.09; 95% CI 1.29, p=0.041). High-titer response at 1-month post-D3 occurred in 29% of D3-JJ recipients and 25% of D3-mRNA recipients (p=0.7); this difference did not reach statistical significance in weighted analysis (wIRR=1.57; 95% CI 0.97, p=0.093). At 3-months post-D3, 80% of D3-JJ recipients and 57% of D3-mRNA recipients were seropositive (p=0.18); D3-JJ recipients were 1.4-fold more likely to be seropositive (wIRR=1.41; 95% CI 1.40, p=0.006). High-titer response at 3-months post-D3 occurred in 27% of D3-JJ recipients and 22% of D3-mRNA recipients (p=0.64); this did not reach statistical significance (wIRR=1.57; 95% CI 0.92, p=0.091). At 6-months post-D3, 88% of D3-JJ recipients and 59% of D3-mRNA recipients were seropositive (p=0.026); D3-JJ recipients were 1.41-fold more likely to be seropositive (wIRR=1.41; 95% CI 1.40, p=0.0028). High-titer response at 6-months post-D3 occurred in 59% of D3-JJ recipients and 21% of D3-mRNA recipients (p=0.005). D3-JJ recipients were 2.63-fold more likely to develop high-titers at 6-months post-D3 compared to D3-mRNA recipients (wIRR=2.63; 95% CI 0.93, p=0.0036). Severe adverse reactions after D3 were rare; one D3-mRNA recipient reported fluid overload temporally associated with SARS-CoV-2 infection. No D3-JJ recipients reported rejection before or after D3. Six D3-mRNA recipients reported acute rejection at median (IQR) 23 (12-131) days before D3.

**Conclusion:** Heterologous vaccination with Ad.26.COV2.S for D3 was associated with higher late serocconversion than homologous vaccination with a third mRNA dose among SOTRs negative after a 2-dose mRNA series. SOTRs with persistent negative sero-response to mRNA vaccine series might benefit from Ad.26.COV2.S as an additional vaccine dose.

---

**Table 1: Demographics**

<table>
<thead>
<tr>
<th>N</th>
<th>Age (y) – mean (SD)</th>
<th>Male – n (%)</th>
<th>Race – n (%)</th>
<th>Black</th>
<th>White</th>
<th>Asian</th>
<th>Other</th>
<th>Time since transplant (y) – mean (SD)</th>
<th>Induction Agent</th>
<th>Anti-thymocyte globulin</th>
<th>Maintenance B regimen</th>
<th>CNI-based</th>
<th>Belatacept-based</th>
<th>Prior SARS-CoV-2 infection – n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>49</td>
<td>54 (13)</td>
<td>30 (79.6)</td>
<td>22 (44.9)</td>
<td>15 (30.6)</td>
<td>2 (4.1)</td>
<td>9 (18.4)</td>
<td>1 (2)</td>
<td>2.2 (6.2)</td>
<td>19 (38.8)</td>
<td>30 (61.2)</td>
<td>Maintenance B regimen</td>
<td>44 (88.8)</td>
<td>5 (10.2)</td>
<td>13 (26.5)</td>
</tr>
</tbody>
</table>

**Table 2: Pre- and post-vaccination clinical parameters**

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Pre-vaccination mean (SD)</th>
<th>Post-vaccination mean (SD)</th>
<th>Difference mean (SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (n=49)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>dd-cfDNA (aDNA)</td>
<td>0.23 (0.18)</td>
<td>0.21 (0.20)</td>
<td>0.02 (0.15)</td>
<td>0.289</td>
</tr>
<tr>
<td>GEP score</td>
<td>9.96 (2.5)</td>
<td>10.4 (2.33)</td>
<td>0.47 (1.23)</td>
<td>0.19 (1.74)</td>
</tr>
<tr>
<td>eGFR</td>
<td>45.65 (18.17)</td>
<td>54.57 (15.23)</td>
<td>0.82 (8.00)</td>
<td>0.0942</td>
</tr>
<tr>
<td>Creatinine</td>
<td>91.5 (12.5)</td>
<td>91.2 (12.0)</td>
<td>0.35 (23.1)</td>
<td>0.922</td>
</tr>
</tbody>
</table>
following financial disclosures: consulting and speaking honoraria from Sanofi, Novartis, CSL Behring, Jazz Pharmaceuticals, Veloxis, Mallinckrodt, Thermo Fisher Scientific, Regeneron, and AstraZeneca. Dr. Levan is the Social Media Editor for Transplantation. Dr. Avery has research support from Acuris, Astellas, Chimerix, Merck, Oxford Immunotec, Qiagen, Regeneron, and Takeda/Shire. The remaining authors of this manuscript have no financial disclosures or conflicts of interest to disclose.

Table 1: Population Characteristics of Solid Organ Transplant Recipients Negative Before Receiving Ad26.COV2.S or BNT162b2/mRNA-1273 as Third Dose of COVID Vaccine

<table>
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<tr>
<th>MHC-deficient CD8+ Tregs as a Universally Compatible Cell Therapy</th>
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<tr>
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Introduction: Adoptive Treg therapy has shown to be effective in a variety of immune diseases in preclinical studies (Bézie et al., Front Immunol. 2017, Blood Adv. 2019) and is currently moving to phase I and II to demonstrate its effectiveness. However, autologous Tregs are expensive and slow to produce, which is why we are considering using ready-to-use allogeneic Tregs for future cell therapy.

Method: CD8+CD4+CD45RC+CD56- T cells were sorted by FACS Aria ll, stimulated with anti-CD3 and CD28 mAbs for 2 days, nucleofected with CRIPR/Cas9 to Knock Out MHC molecules, and cultured for 19 additional days in medium supplemented with rapamycin, IL-2 and IL-15, and stimulated with anti-CD3 and CD28 mAbs every week. Suppression capacity was assessed in vitro on allogeneic CD4+ T cell proliferation in response to third party APCs and in vivo on 1.5 Gy-irradiated NSG mice co-injected with allogeneic human PBMCs. Allogenicity of KO Tregs was assessed on allogeneic CFSE-labeled effector T cells.

Results: First, to explore the feasibility of off-the-shelf CD8+ Treg-cell based therapy, we investigated the capacity of CD8+ Tregs to control allogeneic immune responses. Interestingly, CD8+ Treg could inhibit third-party APC-induced allogeneic T cell proliferation in vitro as efficiently as syn geneic cells. In addition, CD8+ Tregs still control the development of GVHD induced by PBMCs from of foreign donor in vivo in humanized NSG mice. However, as CD8+ Tregs express high levels of MHC-I and -II after ex vivo expansion, we evaluated their immunogenicity against allogeneic T cells. As expected, CD8+ Tregs activated and initiated the proliferation of allogeneic CD8+ and CD4+ effector T cells. Thus, we developed a method to invalidate HLA molecules using CRISPR/Cas9 technology. By targeting B2M and CIITA genes encoding the proteins required for the expression of MHC-I and -II respectively, we succeeded in generating MHC-I and MHC-II deficient CD8+ Tregs with preserved suppressive function, and which, unlike MHC+CD8+ Tregs, did not activate effector T cell proliferation in vitro.

Conclusion: We have shown the therapeutic potential of MHC-deficient CD8+ Tregs for off-the-shelf cell therapy. Experiments are underway to explore the impact of MHC-I deficiency of CD8+ Tregs on their susceptibility to NK cell lysis.

Table 2: Prevalence of Serocorversion comparing Ad26.COV2.S versus BNT162b2/mRNA-1273 as Third Dose of COVID Vaccine Among Solid Organ Transplant Recipients Negative Before Third Dose

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Selective Bcl-2 Inhibition Promotes Hematopoietic Chimerism and Allograft Tolerance Without Myelosuppressive Complications

Takayuki Hirose\(^1\), Hajime Sasaki\(^1\), Tetsu Oura\(^1\), David Ma\(^1\), Grace Laseiter\(^2\), Abbas Dehnadi\(^3\), Isabel Hanekamp\(^3\), Ivy Rosales\(^4\), Robert B. Colvin\(^2\), Benedict A. Coisim\(^1\), Pietro Cippa\(^4\), Thomas Fehr\(^4\), Tatsuo Kawai\(^1\).

\(^1\)Center for Transplantation Sciences, Massachusetts General Hospital, Boston, MA, United States; \(^2\)Pathology, Massachusetts General Hospital, Boston, MA, United States; \(^3\)Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland; \(^4\)Department of Internal Medicine, Cantonal Hospital Graubuenden, Chur, Switzerland.

Introduction: Hematopoietic stem cell transplantation (HSCT) has been an only approach that reproducibly achieved renal allograft tolerance in humans. However, severe myelosuppression and toxicities after myeloablative conditioning have hampered wider clinical application. To achieve hematopoietic stem cell (HSC) engraftment, it is essential to make space in the bone marrow (BM) niches by depleting host HSCs. This has been achievable only by nonselective treatments such as irradiation or chemotherapeutic drugs. Therefore, a novel approach more selectively capable of depleting HSCs is needed to widen the clinical application of HSCT. Based on murine studies that showed successful induction of mixed chimerism and allograft tolerance without irradiation by Bcl-2 inhibition, we evaluated an FDA approved Bcl-2 inhibitor (Venetoclax, Vntx) in our mixed chimerism inducing conditioning regimen.

Methods: Cynomolgus monkeys received kidney and bone marrow transplantation after conditioned with various nonmyeloablative regimens which included total body irradiation (TBI), thymic irradiation (TI) and anti-thymocyte globulin (ATG), followed by a short post-transplant course of costimulatory blockade (CoB) and Cyclosporine. The study groups were consisted of 3Gy TBI, no Vntx (Group A), 1.5Gy TBI, no Vntx (Group B), TBI 1.5Gy with Vntx (10 mg/kg x 11 on days -4 to 6) (Group C), TBI 1.5Gy with Vntx but Belatacept as CoB (Group D), no TBI with Vntx (Group E), no TI with Vntx (Group F), no CoB with Vntx (Group G).

Results: Most recipients treated with 3Gy TBI (Group A) developed mixed chimerism and long-term immunosuppression (I.S.)-free renal allograft survival (Table 1), but suffered from transient but severe pancytopenia. With reduced TBI (1.5Gy), all recipients failed to develop chimerism, and 4/5 developed acute rejection. By adding Vntx, despite the dose of TBI being reduced to half (1.5Gy), all six recipients (Group C) developed significantly superior chimerism (Figure 1) than regimens without Bcl-2 inhibition (Groups A and B), and 5/6 achieved long-term I.S.-free allograft without pancytopenia (Figure 2). With Belatacept in place of anti-CD154 mAb, 2/3 achieved chimerism and long-term I.S. free allograft survival. The current studies also revealed that a minimal non-toxic dose of TBI, TI and CoB remain to be essential for long-term I.S.-free renal allograft survival. Without TBI (Group E) or CoB (Group G), the recipients failed to develop chimerism and rejected allografts despite administration of Vntx. Without TI (Group F), all recipients developed mixed chimerism but failed to achieve tolerance.

Conclusion: Bcl-2 inhibition with Vntx significantly promoted mixed chimerism and renal allograft tolerance without myelosuppressive complications. A minimal non-toxic dose of TBI, TI, and CoB were still required for chimerism and allograft tolerance induction even with Bcl-2 inhibition.

Table 1. The regimen and renal allograft survivals in each group

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Bcl-2</th>
<th>TBI (Gy)</th>
<th>TI (Gy)</th>
<th>CoB</th>
<th>Renal Allograft Survival (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>6</td>
<td>-</td>
<td>3</td>
<td>7</td>
<td>acCD154</td>
<td>4328, 2498, 837, 755, 401, 373, 206, 58</td>
</tr>
<tr>
<td>B</td>
<td>5</td>
<td>1.5</td>
<td>7</td>
<td></td>
<td>acCD154</td>
<td>&gt;1009, 167, 112, 160, 58</td>
</tr>
<tr>
<td>C</td>
<td>6</td>
<td>+</td>
<td>1.5</td>
<td>7</td>
<td>acCD154</td>
<td>&gt;1657, &gt;1911, &gt;2526, &gt;313, &gt;287, 127</td>
</tr>
<tr>
<td>D</td>
<td>3</td>
<td>+</td>
<td>1.5</td>
<td>7</td>
<td>Belatacept</td>
<td>&gt;749, 603, 237</td>
</tr>
<tr>
<td>E</td>
<td>2</td>
<td>+</td>
<td>7</td>
<td></td>
<td>acCD154</td>
<td>142, 120</td>
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<tr>
<td>F</td>
<td>3</td>
<td>+</td>
<td>1.5</td>
<td>7</td>
<td>acCD154</td>
<td>163, 100, 97</td>
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<tr>
<td>G</td>
<td>3</td>
<td>+</td>
<td>1.5</td>
<td>7</td>
<td>-</td>
<td>161, 127, 74</td>
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</tbody>
</table>
Anti-C4d Chimeric Antigen Receptor Regulatory T Cells Suppressed Allograft Rejection in ABO-Incompatible Heart Transplantation

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Introduction: Antibody-mediated rejection (ABMR) is the main hurdle in ABO blood group-incompatible (ABOi) transplantation. C4d deposition is a marker of ABMR and is also found in most ABOi allograft tissues as a result of accommodation. Previously, we reported that anti-C4d chimeric antigen receptor (CAR) regulatory T cells (Tregs) suppressed ABMR in ABOi allografts. Here, we aimed to improve efficacy of anti-C4d CAR Tregs by modifying CAR structure and increasing dose of CAR Tregs.

Methods: Intracellular costimulatory domains of anti-C4d CAR Treg consisted of mouse CD3ζ and CD28. CD62L+CD4+CD25+ T cells were sorted and transduced with retroviral CAR using retronectin on two consecutive days. We assessed in vitro suppressive function of anti-C4d CAR Tregs against T cell proliferation in response to polyclonal stimulation. Wild-type C57BL/6J mice were sensitized on day -21 and on day -14 by injecting human blood group A-expressing cells. Hearts from human blood group A-transgenic BALB/c mice were transplanted into the sensitized CD45.2+ C57BL/6J mice to make an anti-ABO antibody-mediated rejection model. CD45.1+ non-transduced, control CAR, or anti-C4d CAR Tregs (1×10^6) were transferred into recipient mice on day-1 and day 2 after transplantation in combination with prednisolone, tacrolimus, and rapamycin. ABOi heart allograft were analyzed for tissue damage, cellular infiltration, and cytokine expression on day 7.

Results: Anti-C4d CAR Tregs express Foxp3, CD25, CTLA-4, LAP, and GITR that are associated with immunosuppressive functions of Tregs, to similar extent as either nontransduced or control CAR Tregs. In vitro suppressive activity of anti-C4d CAR Tregs was also similar as that of nontransduced Tregs and control CAR Tregs. ABOi heart allografts showed typical features of ABMR, such as, peritubular capillitis and diffuse endothelial C4d+ deposition. Adoptive transfer of anti-C4d CAR Tregs suppressed ABMR-related tissue injury and significantly prolonged ABOi heart allograft survival compared to PBS control group, nontransduced Treg group, and control CAR Treg group. Both flow cytometric analysis and immunofluorescence imaging study demonstrated that number of CD45.1+Foxp3+ Treg infiltration into heart allograft were significantly higher in anti-C4d CAR Treg group compared to PBS control, nontransduced CAR Treg group, and control CAR Treg group. Expression of IL-2, TNF-α, and IFN-γ in heart allografts was significantly lower in anti-C4d CAR Treg group than PBS control group.

Conclusions: Anti-C4d CAR Tregs infiltrated into ABOi heart allograft with diffuse C4d deposition to more extent and thereby suppressed ABMR in ABOi heart allografts more effectively, compared to nontransduced Tregs and control CAR Tregs.

Keywords: ABO-incompatible transplantation; C4d; Chimeric antigen receptor; Regulatory T cells; Rejection.
Mitochondrial Complex V Inhibition Enhances Human Regulatory T Cell Suppressive Function Through the Induction of Immunosuppressive Small Extracellular Vesicles

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Introduction: Regulatory T cells (Tregs) have a critical role in immune tolerance. Clinical trials of autologous in vitro expanded Tregs therapy have demonstrated promising preliminary results, but there remain challenges to overcome including the donor-dependent in vitro expansion potential and time required for preparation. Here, we revealed that mitochondrial complex V inhibition enhances Treg suppressive function through the induction of immunosuppressive small extracellular vesicles which act in donor-independent manor.

Methods: Human CD4+CD25+CD127lo/- Tregs were flow sorted from peripheral blood mononuclear cells of healthy donors and expanded for two weeks in vitro in the presence of anti-CD3/anti-CD28 beads. Expanded Tregs were pre-treated by mitochondrial complex V inhibitor prior to the in vitro suppression assay to assess their suppressive function. To assess immunosuppressive soluble molecules, Treg culture supernatants were collected. To further identify these molecules, 100kDa ultracentrifugation filter and small extracellular vesicles depletion kits were applied to the supernatant prior to adding to T cell proliferation assay.

Results and Discussion: Mitochondrial complex V inhibitor pretreatment dramatically enhanced Treg suppressive function (Fig 1.a). However, pretreated Tregs did not increase their expression of known immune regulatory markers such as CTLA-4, PD-1, CD39 and CD25. We therefore hypothesized that pretreated Tregs produced immunosuppressive soluble molecules. Confirming this, Treg culture supernatants possessed strong suppressive function (Fig 1.b). Whilst pretreated Tregs produced higher levels of IL-10, only the >100kDa fraction of the culture supernatant showed strong suppressive potential, indicating that the responsible suppressive factor was likely to be extracellular vesicles. Removal of small extracellular vesicles using either silicon carbide-based exosome removal kit (Fig 2.a) or anti-CD9, CD63 and CD81 magnetic beads (Fig 2.b) diminished the immunosuppressive properties of the pretreated Tregs culture supernatants, directly proving that Tregs produce immunosuppressive small extracellular vesicles after mitochondrial complex V inhibition. Lastly, we revealed that these immunosuppressive small extracellular vesicles suppressed 3rd party T cell proliferation (Fig 2.c).

Conclusions: This study reveals that pretreatment of pharmacological mitochondrial V complex inhibition can be used to enhance in vitro expanded Tregs function to reduce the required dose in Treg cellular therapy. Moreover, the donor-independent function of the small extracellular vesicles derived from mitochondria complex V inhibitor-treated Tregs may provide a new potential therapeutic strategy in which small extracellular vesicles could be used ‘off-the-shelf’.
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**Anti-CD40L Antibody Promotes the Differentiation of Vγ2+ Regulatory Gamma-delta T Cells and Prolongs the Survival of Skin Allografts**

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**Introduction:** The effector function of gamma-delta (γδ) T cells are well characterized in several infections, autoimmunity, and tumor model. The role of γδ T cells and their regulatory function in transplantation is well characterized.

**Method:** C57BL/6 mice (H-2b) were given donor-specific transfusion (DST; 10 X 10^6 cells/mouse on day 0) and anti-CD40L mAb (clone MR1; 250 μg/injection/mouse on -3, -1, +1, +4 day relative to transplantation) and transplanted BALB/c mice (H-2d) skin allografts. Flow cytometry analysis showed that depleting Vγ2+ T cells reduced the frequency of Foxp3+CTLA4+ regulatory T cells in the secondary lymphoid organs. To deplete the total γδ T cells or Vγ2+ T cells, recipient mice were given intravenous injection (200 μg/mouse/injection) of anti-mouse γδ TCR mAb (clone UC7-13D5) or anti-mouse TCR Vγ2 mAbs (clone UC5-19A8) 3 x 10^4 cells/mouse on day -7, -4, 0, and +4 day relative to transplantation and transplanted BALB/c mice (H-2d) tail-skin allografts. Graft survival was monitored. To deplete the total γδ T cells or Vγ2+ T cells, recipient mice were given intravenous injection (200 μg/mouse) of anti-mouse γδ TCR mAb significantly reduced the tolerogen-induced survival of allografts (MST 15.5 days). Flow cytometry analysis showed that depleting Vγ2+ T cells reduced the frequency of Foxp3+ cells and secretion of inflammatory cytokines (IL-17 and IFN-γ) or regulatory cytokine IL-10 in total γδ T cells in the thymus, spleen, and lymph nodes. Further analysis showed that tolerogen treatment significantly increased the frequency of γδ T cells in the splenocytes, and lymph nodes. Tolerogen treatment promoted CD309Vγ2+ γδ T cells and suppressed IFN-γ production in Vγ2+ γδ T cells in the spleen, lymph nodes, and allografts. Vγ2+ γδ T cells isolated from tolerized mice suppress in vitro differentiation of Th1 cells. Depletion of only Vγ2+ γδ T cells with anti-Vγ2-specific mAb prevented tolerogen-induced survival of allografts (MST 15.5 days). Flow cytometry analysis showed that depleting Vγ2+ γδ T cells reduced the frequency of Foxp3+ T cells in the secondary lymphoid organs and allografts. This rise was specific to only only allografts but not to the syngeneic grafts in the same recipients. Furthermore, the adoptive transfer of only purified Vγ2+ γδ T cells from the tolerogen-treated mice to naïve TCR δ- (H-2d) recipient mice prolonged the survival of BALB/c skin allografts.

**Conclusion:** Vγ2+ γδ T cells promote the survival of allografts and can be used as an adoptive cellular therapy to prolong the survival of allografts in a transplantation setting. This work was supported from the grants from the Department of Biotechnology (Grants numbers, BT/PR15533/MED/30/1616/2016; BT/PR14156/BBR/10/1515/2016), and Department of Science and Technology (DST/SIF/LSA-01/2017-18), Government of India.

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**Tolerance of Allogeneic Kidneys With Durably (>365 Days) Multilineage Chimerism and Bone Marrow Engraftment in Cynomolgus Macaques**

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**Background:** We have previously reported that a regimen including anti-CD3 immunotoxin, cyclosporine, and pre-transplant total body irradiation (TBI) promoted tolerance of kidney allografts and enabled complete withdrawal of immunosuppression with transient chimerism in non-human primates. Donor islets were also tolerated when transplanted in composite islet-kidney (IK) grafts. However, data from a rodent model demonstrated that durable chimerism may be required to reverse the autoimmune responses associated with diabetes in the absence of immunosuppression. In this study, we aimed to develop a clinically applicable protocol to induce tolerance of allogeneic kidneys with >6 months durable chimerism in NHPs.

**Methods:** Cynomolgus macaques received one-haplotype mismatched, mobilized peripheral blood hematopoietic stem cell transplantation (PBHSCTx) on Day 0 followed by donor kidney Tx (DKTx) on Day 42. Recipients in Group 1 (n=5) received PBHSCTx that contained 3.7-20x10^7 CD34+ cells/kg recipient body weight (bwt), recipients in Group 2 (n=5) received PBHSCTx containing a lower dose of CD34+ cells (2x10^7 cells/kg bwt). All recipients received Rituximab, rATG, and 100× Gy of TBI before PBHSCTx. Tacrolimus was administered daily starting on Day -1 and was stopped at Day 41 after PBHSCTx. Anti-CD40mAb was administered twice weekly until 30 days after DKTx (72 days after PBHSCTx).

**Results:** All animals developed and maintained multilineage chimerism with evidence of bone marrow (BM) engraftment throughout the experimental period. However, all animals who received PBHSCTx with high numbers of CD34+ cells (Group 1) were euthanized due to GVHD or cytokine storm at early time points (Days 33, 43, 45, 55, 92). In contrast, recipients who underwent PBHSCTx with lower numbers of CD34+ cells at 2x10^7 cells/kg bwt (Group 2) had no evidence of GVHD or cytokine storm and had significantly prolonged survival (p<0.02). Although two animals were euthanized at Day 118 and 218 days due to CMV infection, all animals who received PBHSCTx with high numbers of CD34+ cells (Group 1) were euthanized due to GVHD or cytokine storm at early time points (Days 33, 43, 45, 55, 92). In contrast, recipients who underwent PBHSCTx with lower numbers of CD34+ cells at 2x10^7 cells/kg bwt (Group 2) had no evidence of GVHD or cytokine storm and had significantly prolonged survival (p<0.02). Although two animals were euthanized at Day 118 and 218 days due to CMV infection, all animals maintained macrochimerism throughout the experimental period. All animals who received appropriate CMV therapy had stable clinical courses, and accepted kidneys (two from actual HSCTx donors and one from a donor with Class II DRx matched to the HSC donor) that were transplanted 42 days after PBHSCTx without any episode of rejection crisis (currently >368, >194 and >143 days). Notably, the longest-term follow-up animal (>368 days) maintains multilineage peripheral chimerism as well as clear BM chimerism. Furthermore, in vitro data showed donor-specific unresponsiveness in vitro and donor-derived recent thymic emigrants.

**Conclusions:** To our knowledge, this is the first demonstration of reproducible, >365 days multilineage durable chimerism with BM engraftment and kidney graft tolerance in a cynomolgus HSCTx and kidney Tx model. Achieving long-term durable (>6 months) chimerism, which may be a goal of curing T1D and diabetic nephropathy by transplantation of IKs, we aimed to develop a clinically applicable protocol to induce tolerance of allogeneic kidneys with >6 months durable chimerism in NHPs.
Donor-derived Cell-Free DNA Testing in Kidney Transplantation: Do One-month Values Have Any Prognostic Significance?

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Introduction: Percutaneous renal allograft biopsy is the current standard for detecting acute rejection after kidney transplantation (KT). Noninvasive tests such as plasma-based donor-derived cell-free DNA (dd-cfDNA) assays have been proposed as an alternative to biopsy. We sought to examine the value of dd-cfDNA testing at one month following KT in different donor and recipient categories.

Methods: We performed a single center retrospective review of all adult KT patients (pts) who underwent dd-cfDNA testing between January 2018 and August 2021. The diagnosis of acute rejection was based on histopathology obtained from percutaneous, ultrasound-guided needle biopsies. Our center’s standard practice included dd-cfDNA testing and performing surveillance kidney biopsies at 1 month following KT. The dd-cfDNA test was considered elevated if >1%.

Results: During the study period, 3157 dd-cfDNA tests were performed in 695 de novo pts. Higher mean 1-month dd-cfDNA levels were noted in the following categories: Retransplants (n=30, 1.8±2.1); highly sensitized pts (PRA 98-100%, n=27, 1.6±2.0); for highly sensitized retransplants, n=18, 2.0±2.3; for highly sensitized primary KTs, n=9, 0.7±0.5; and pts who underwent early reoperations (n=16, 0.85±0.9). In all other KT categories, mean 1-month dd-cfDNA levels were lower and similar: DCD donor KTs (n=53, 0.56±0.4); living donor KTs (n=51, 0.47±0.4); acute kidney injury (AKI) donor KTs (n=23, 0.47±0.6); standard criteria donor (SCD) KTs (n=91, 0.47±0.4); expanded criteria donor (ECD) KTs (n=44, 0.46±0.5); dual KTs (n=16, 0.45±0.4); and pts with delayed graft function (DGF, n=50, 0.46±0.4). In 58 primary KT pts with negative 1-month surveillance biopsies, corresponding mean 1-month dd-cfDNA levels were 0.49±0.4. In 10 pts with positive 1-month surveillance biopsies, corresponding mean 1-month dd-cfDNA levels were 1.5±1.8. In 26 pts with a 1-month dd-cfDNA level >1.0, the subsequent incidence of acute rejection was 27%; in 22 pts with a 1-month dd-cfDNA level ≥2.0, the subsequent incidence of acute rejection was 50% (mean follow-up 14 months).

Conclusions: We noted a bimodal distribution of 1-month dd-cfDNA levels. Higher mean 1-month dd-cfDNA levels (range 0.72-2.2) were associated with retransplants, high PRA pts, and pts with early reoperations; 22-44% of these pts had 1-month dd-cfDNA levels >1.0. Conversely, primary KT alone pts (DCD, living donor, AKI donor, SCD, ECD, dual KT, those with DGF) had lower 1-month dd-cfDNA levels (range 0.45-0.56) and only 7-14% had 1-month dd-cfDNA levels >1.0. One-month surveillance biopsy results correlated with corresponding dd-cfDNA levels. Elevated 1-month dd-cfDNA levels occurred in pts at a higher risk for acute rejection, suggesting that these pts need to be monitored more closely.

High Levels of Donor Derived Cell-Free DNA in the Early Post-transplant Phase Indicates Injury Independent of Renal Function Status

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Background: More than 97,000 patients are in the wait list for a kidney transplant in the United States, but only 24,670 transplants were performed in the year 2021. While living donation remained nearly steady in the last 10 years, deceased donation increased 40%. Donation after circulatory death (DCD) donors are a progressively important source of organs. However, DCD donor kidneys have an increased risk of slow (SGF) and delayed graft function (DGF). Patients with DGF often undergo multiple biopsies to differentiate between ischemic acute tubular injury and rejection to prevent early graft loss. Donor derived cell-free DNA (dd-cfDNA) is a non-invasive biomarker for detection of graft injury and rejection in kidney transplant. This study aims to assess the association of dd-cfDNA levels with immediate post-transplant graft function, biopsy proven rejection and rejection treatment in patients with SGF and DGF.

Methods: In this observational single-center study we identified 70 deceased donor kidney transplant recipients at the Miami Transplant Institute with dd-cfDNA testing in the first 30 days after transplantation. Of those, 18 patients had a paired dd-cfDNA and for cause biopsy. Indications for biopsy were creatinine >2ml/dl, donor specific antibodies (DSA), proteinuria, dd-cfDNA levels >1%. Patients were grouped according to allograft function status as DGF, SGF or immediate graft function (IGF). Median dd-cfDNA levels were evaluated in comparison to graft function, biopsy proven rejection, and treatment after rejection, and compared by Kruskal Wallis test between each categorized group. P <0.05 was considered significant.

Results: 38.8% of patients received a DCD kidney with a mean KDPI of 58% (±29.8). 27.8% of patients were female. 9 patients had DGF, six had SGF and 3 had IGF. There was no difference in median dd-cfDNA levels between the groups in the first 20 days of transplant Figure 1A. There was no difference in rejection occurrence between the groups. Patients with active rejection had higher levels of dd-cfDNA compared with patients with no rejection and chronic antibody mediated rejection (Figure 1B). When evaluating treatment for rejection, patients that underwent treatment had a significant reduction in dd-cfDNA levels post-treatment (Figure 1C). 7 patients with borderline rejection did not receive treatment, the median dd-cfDNA was 0.37% (range – 0.16-1.3%), while patients with borderline rejection and treatment had 1.3% median dd-cfDNA (range – 0.44-1.7%; p=0.015).

Conclusions: High levels of dd-cfDNA were associated with allogimmune injury irrespective of graft function, showing the clinical utility of this biomarker in the early post-transplant. Patients with DGF are more prone to develop allograft injury, but all patients may benefit of close surveillance in the early post-transplant period. Further evaluation is needed to elucidate the benefits of dd-cfDNA surveillance over biopsy in this clinical setting.
Longitudinal Analysis of Donor-derived Cell-Free DNA (Dd-cfDNA) in En-bloc Kidney Transplantation

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Introduction: The longitudinal dd-cfDNA patterns in en-bloc kidney transplant recipients have not been studied. It is unknown how the initial smaller mass of the two pediatric organs impacts dd-cfDNA early post-transplant or if the dd-cfDNA rises over time as the organs enlarge. We analyzed dd-cfDNA scores over the first 12 months in recipients of pediatric en-bloc kidneys enrolled in the Kidney allograft Outcomes AlloSure Registry (KOAR, NCT03326076).

Methods: 16 recipients of pediatric en-bloc kidneys with donors aged ≤7 years old were identified and compared with 931 single, non-en-bloc deceased donor recipients. Patients with rejection were excluded.

Results: Of the 16 en-bloc recipients, 56.2% were male with median donor age of 1.4 years and median cold ischemia time (CIT) of 20 hours. None of the en-bloc transplants had delayed graft function. Aside from KDPI, donor age, and recipient age, no other differences were observed between groups (Table 1).

Higher median dd-cfDNA values were seen in the en-bloc cohort compared to not en-bloc at month 1 (M1, 1.4% vs 0.4%) and month 2 (0.58% vs 0.23%) after transplant (p<0.001) (Figure 1a). Median dd-cfDNA values were comparable for month 3 (0.21% vs 0.16%, p = 0.07) and all subsequent time points (Figure 1a, 1b). Among 8 patients with M1 dd-cfDNA results, there was no significant association between M1 dd-cfDNA and either CIT (r=0.33, p=0.419) or KDPI (r=-0.23, p=0.589) (Figure 2).

Conclusion: Our results demonstrate higher early post-transplant dd-cfDNA values among en-bloc kidney compared to single kidney recipients however, no difference or upward trend is observed beyond month 2 and out to 12 months.

Table 1. Demographics

<table>
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<th>Total</th>
<th>Not En-Bloc</th>
<th>En-Bloc</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Total Number of Patients</td>
<td>947</td>
<td>931</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>947</td>
<td>931</td>
<td>16</td>
<td>0.0287</td>
</tr>
<tr>
<td>Median (range)</td>
<td>57 (21, 84)</td>
<td>57 (21, 84)</td>
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<tr>
<td>Induction Immunosuppression</td>
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<td>931</td>
<td>16</td>
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<tr>
<td>ATG</td>
<td>692 (73.1%)</td>
<td>679 (72.9%)</td>
<td>13 (81.2%)</td>
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<tr>
<td>Alemtuzumab</td>
<td>121 (12.8%)</td>
<td>118 (12.7%)</td>
<td>3 (18.8%)</td>
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<tr>
<td>Basiliximab</td>
<td>87 (9.2%)</td>
<td>87 (9.3%)</td>
<td>0 (0%)</td>
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</tr>
<tr>
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<td>47 (5%)</td>
<td>47 (5%)</td>
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<td></td>
</tr>
<tr>
<td>Donor Age</td>
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<td>896</td>
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<td>Median (range)</td>
<td>41 (0, 75)</td>
<td>41 (2, 75)</td>
<td>1.4 (0, 5)</td>
<td></td>
</tr>
<tr>
<td>25th - 75th</td>
<td>30 - 52</td>
<td>30 - 52</td>
<td>0.52 - 2</td>
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<tr>
<td>KDPI</td>
<td>888</td>
<td>872</td>
<td>16</td>
<td>&lt;0.0001</td>
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<tr>
<td>Median (range)</td>
<td>52 (1, 100)</td>
<td>52 (1, 100)</td>
<td>80 (46, 92)</td>
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<tr>
<td>Cold Ischemia Time (hours)</td>
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<td>838</td>
<td>15</td>
<td>0.3406</td>
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<tr>
<td>Median (range)</td>
<td>17 (0, 45)</td>
<td>17 (0, 45)</td>
<td>20 (6, 34)</td>
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</table>
Donor-derived Cell-free DNA (Dd-cfDNA) for Assessment of Response After Treatment of Allograft Rejection

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Introduction: Surveillance of dd-cfDNA after therapy for rejection represents a promising strategy for monitoring post-treatment response. We assessed post-rejection kinetics of dd-cfDNA among kidney transplant recipients in the Kidney allograft Outcomes AlloSure Registry (KOAR, NCT03326076).

Methods: We identified patients with biopsy-proven allograft rejection (BPAR), defined as ABMR, TCMR, or Mixed (Banff 2019), biopsy-paired dd-cfDNA measurements (within ≤30d of biopsy), and follow-up results 60-150 days after BPAR. When available, treatment and follow-up histology data was also analyzed.

Results: 48 episodes of BPAR (24 TCMR, 19 ABMR, 5 Mixed) and paired dd-cfDNA results were identified in 42 patients (Table 1). Overall, a significant reduction was seen between the median index (1.36%, IQR: 0.29-2.25) and follow-up dd-cfDNA results (0.35%, IQR: 0.13-0.95; p < 0.01) (Figure 1a). For patients with concurrent eGFR measurements, no statistically significant improvement was seen. These patterns held when analysis was limited to TCMR and ABMR/Mixed rejections (Figure 1b, 1c). 7 patients (2 ABMR, 4 TCMR, and 1 Mixed; median index dd-cfDNA 1.15%, IQR: 0.31-2.46) had repeat biopsies within 30 days of their follow-up testing; 1 patient with acute ABMR had chronic active ABMR on repeat biopsy, with a dd-cfDNA of 1.86%, while the remainder had either no rejection or borderline findings (median dd-cfDNA 0.74%, IQR: 0.30-2.59).

Conclusions: Our findings highlight that reduction in dd-cfDNA is commonly seen following BPAR, suggesting that most patients experience a “molecular response” to therapy. Studies are needed to better understand the prognostic significance of a molecular response and how persistent elevations in dd-cfDNA after treatment should guide subsequent management.

Table 1:

<table>
<thead>
<tr>
<th>Index Biopsies with Paired dd-cfDNA (n = 48)</th>
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<tbody>
<tr>
<td>TCMR</td>
</tr>
<tr>
<td>1A</td>
</tr>
<tr>
<td>1B</td>
</tr>
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<td>2A</td>
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<td>2B</td>
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<table>
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<tr>
<td>Acute</td>
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<tr>
<td>Chronic Active</td>
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<tr>
<td>Suspicious for ABMR (+/- borderline TCMR)</td>
</tr>
<tr>
<td>Mixed ABMR/TCMR</td>
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</tbody>
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Identification of the Source of Donor Derived Cell-free DNA in A Kidney-pancreas Transplant Recipient: Case Study

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Although outcomes of Kidney-Pancreas Transplant (KPT) have steadily improved over the years rejection remains the primary cause of graft loss after 3 months. The surveillance for graft rejection is done by serum creatinine, for the kidney, and pancreatic enzymes for the pancreas. Both can be non-specific to graft injury. Donor derived cell-free DNA (dd-cfDNA) is a non-invasive biomarker recently added to the standard of care of many transplant centers to monitor for rejection in Kidney Transplant (KT) recipients. The use of dd-cfDNA in KPT brings some challenges since it is typically not possible to identify organ source of elevated dd-cfDNA without genotype information. Additionally, when a second KT is necessary after the failure of a first kidney, in the context of keeping the pancreas, then genotypes of both donors and recipient are typically required to identify organ source. Here we report the application of a novel algorithm that does not require genotyping of both donors, to evaluate the levels of each dd-cfDNA in a KPT recipient who had a second KT. A 50-year-old female received a KPT in 2012 from a deceased donor. Since this was a bladder drained pancreas transplant, urine amylase was followed in addition to creatinine and pancreatic enzymes. Patient developed kidney chronic rejection and received a second living donor KT in 2018 with removal of the original KT in the same operation. The pancreas transplant continued to function well. 2 years later a biopsy of the second KT demonstrated TCMR IB, IIA. After treatment with steroids pulse, patient was surveilled with AlloSure® dd-cfDNA. Although, no clinical signs of rejection, dd-cfDNA showed high variability over time (Figure 1). A second kidney biopsy was performed showing borderline rejection. Patient was treated with steroids pulse but developed donor specific antibodies (DSA). To avoid a pancreas biopsy, we obtained DNA material from the recipient and from the donor of the second KT to determine if the elevated levels of dd-cfDNA was from injury to the pancreas. A novel algorithm was used to differentiate the SNPs (Single Nucleotide Polymorphisms) from donor 1 (1st KPT and donor 2 (KT). We were able to determine that most dd-cfDNA was being released by the 2nd kidney transplant, but both organs showed high variability over time (Figure 2). High variability in dd-cfDNA serial results is usually linked with non-adherence or improper intake of immunosuppressive drugs. Also, the presence of de novo DSA is associated with increase in dd-cfDNA and both combined over time with poor long outcomes. There is a need for more specific non-invasive biomarkers in dual organ transplantation. dd-cfDNA in surveillance of rejection in KPT has shown to be a useful tool. The ability to identify the specific organ source of the injury allows for the reduction of unneeded biopsies and better clinical management.
Assessment of Donor Derived Cell Free DNA (ddcfDNA) at Surveillance and at Clinical Suspicion of Acute Rejection in Renal Transplantation

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Introduction: In order to study the efficacy of less pervasive methods to screen patients after renal transplantation, we tried to assess the correlation between ddcfDNA and acute rejection, cellular (TCMR) or antibody mediated rejection (ABMR) in recipients of renal allograft.

Method: Two groups of renal transplanted patient were assessed. The first group contained newly transplanted patients, from whom samples were collected at month 1, 2, 3 & 5 for ddcfDNA analysis, along with creatinine/eGFR and DSA monitoring. The second group was consisted of patients who underwent a renal biopsy for any cause and whose ddcfDNA were measured at the time of biopsy and 4 weeks afterwards. The biopsy group was further divided in two subgroups, patients diagnosed with rejection (ABMR and TCMR) and patients without rejection. Levels of ddcfDNA were also compared to serum creatinine and eGFR levels. The follow up of the patients lasted for one year. Measurements of dd-cfDNA were done using AlloSeq cfDNA kit (CareDx).

Results: The first group contained 30 patients (13 males), mean age 46.5±10.8 years, 6 patients who underwent ABO incompatible transplantation and 7 with preformed DSA. The second group was consisted of 32 patients (21 males), mean age 41.5±14.3 years, 7 patients who underwent ABO incompatible transplantation and 14 with preformed DSA. There was a statistical significance in ddcfDNA between patients who were diagnosed with acute rejection (median value 0.94%, IQR 0.3-2) and those without rejection (0.24% IQR 0.2-0.34) (p=0.004), while there was no significant difference in the serum creatinine. When a ddcfDNA threshold of 0.5% was chosen, it had a sensitivity of 73.7% and a specificity of 92.3% for the diagnosis of rejection (AUC: 0.80, 0.65-0.96) (Fig.1). Significant difference in ddcfDNA was also noticed among patients with ABMR (median value 13%, IQR 1.3-16), those with TCMR (0.52%, 0.23-1.70) and those without rejection (0.24%, 0.20-0.34) (p=0.0014). No difference was found in ddcfDNA among patients with borderline rejection, TCMR1 or TCMR2. When looking at newly transplanted patients with persistently elevated ddcfDNA (AlloSeq >1 result, ≥0.5%), the ddcfDNA level cut-off of 0.5% was not able to predict any difference in eGFR from month 5 to month 12. Finally, levels of ddcfDNA in the rejection subgroup before biopsy (0.94%, 0.3-2.0) decreased significantly after initiation of treatment with median returning to baseline already at 1 month (0.33%, 0.21-0.51, p=0.0036) (Fig.2).

Conclusion: Our study shows that ddcfDNA is a reliable biomarker for the diagnosis and monitoring of treatment of acute rejection, especially of antibody mediated rejection, as well as a useful screening tool for the patients who will require a renal allograft biopsy in the future.

Figure 1 ROC analysis. Diagnostic accuracy of ddcfDNA and serum creatinine in relation to biopsy proven rejection at month 0 (time of biopsy and diagnosis) in renal recipient patients. AUC: area under the curve; CI: confidence interval.

Figure 2 ddcfDNA kinetics with anti-rejection treatment. Total of 15 patients with biopsy and rejection (antibody-mediated rejection (ABMR) or T cell-mediated rejection (TCMR)). Values shown are at month 0 (time of biopsy and diagnosis), and at 1 and 2 months (after rejection treatment was initiated). For the sake of clarity, 4 patients with high levels of ddcfDNA (>2.0%) were excluded from the graph presented. Each diamond represents a biopsy specimen. Levels of ddcfDNA at month 0 (0.94%, 0.3-2.0) decreased substantially after initiation of treatment with median returning to baseline already at 1 month (0.33%, 0.21-0.51, p=0.0036). The difference was even more significant when comparing median ddcfDNA levels at month 2 (0.19%, 0.12-0.33) to median levels at month 0 (p=0.0007).

CareDx.
Elevated Donor-Derived Cell-Free DNA Associates With Subsequent Decline of Allograft Function

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Introduction: Donor-derived cell-free DNA (dd-cfDNA) emerged as a candidate biomarker for detecting graft injury, particularly from antibody-mediated rejection, and is currently proposed to complement donor-specific antibodies (DSAs) as an alloimmunemediated injury surveillance method. We sought to investigate the impact of an initial increase of dd-cfDNA level on subsequent decline in graft function.

Materials: The study included all kidney transplant (KT) recipients that underwent dd-cfDNA testing as part of their clinical care between September 2017 and December 2019 at our center. Only patients with a follow-up of at least 12 months were included in this analysis. An elevated dd-cfDNA was defined as a level over 0.5%.

Results: Of the 171 KT recipients tested for dd-cfDNA, 49 were followed for at least 12 months since initial testing. The study cohort had an initial serum creatinine and eGFR of 1.64 ± 0.58 mg/dl and 48 ± 21 ml/min/1.73 m2, respectively. Overall, the absolute and percentual decline of eGFR were −0.12 ml/min/month (IQR, −0.43 to 0.56) and −4.26% (IQR, −20.5% to 17%), with 26.5% and 10.2% of patients having an eGFR decline of more than 15% and 30%, respectively. Fifteen patients (30.6%) had an elevated dd-cfDNA level over 0.5% and had a similar baseline allograft function compared to those without an elevated dd-cfDNA level. After a median follow-up period of 15.3 months (IQR: 13.6–19), patients with elevated dd-cfDNA had a faster decline of eGFR [absolute eGFR decline, −0.21 ml/min/month (IQR, −0.36 to 0.22); percentual GFR decline, −8.7% (IQR, −25% to 4.4%)], compared to those without elevated dd-cfDNA [absolute eGFR decline, +0.03 ml/min/month (IQR, −0.5 to 0.6); percentual GFR decline, +1.14% (IQR, −14% to 28%)] (p=0.09)(Figure 1). Similarly, there was a tendency for a higher percentage of patients with elevated dd-cfDNA for a decline of eGFR greater than 15% (33.3% vs. 23.5%, p=0.5) or 30% (13.3% vs. 8.8%, p=0.0), respectively. In addition, patients with DSAs and an elevated dd-cfDNA showed a greater percentual eGFR decline (−9.1 ± 16.5%), compared to those with DSAs and normal dd-cfDNA (+2.3±18.05%), or to those without DSAs and normal dd-cfDNA (+3.3±21.1%). In multivariable logistic regression analysis, an elevated dd-cfDNA level was independently associated with the subsequent percentual decline of eGFR (OR, 0.96; 95%CI, 0.93 to 1.00; p=0.05).

Conclusion: Measurement of dd-cfDNA in the early post-transplantation period showed decline kinetics at day 30 compared to day 15, reaching stable baseline at day 90. Although discrimination between rejection or infection in contrast to stable allograft was already observed at day 30, dd-cfDNA surveillance may be a clinically useful tool for the assessment of lung allograft function and rule out of injury when patient achieves baseline, which in our cohort observed to happen between day 30 and 90.

Donor-Derived Cell-Free DNA Surveillance Level Kinetics After Lung Transplantation: Experience From a Single-Center Feasibility Study

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Introduction: Previous longitudinal observational studies have described increases of donor-derived cell-free DNA (ddcfDNA) in lung transplant acute rejection and infection, supporting its use as a potential non-invasive marker for surveillance monitoring. Here we present the preliminary data of a feasibility study for implementing ddcfDNA in routine clinical care at our lung transplant center with test performed in house.

Method: Single-center observational study including 45 newly adult lung transplant patients (>18 years old) followed at the CHU Hôpital Nord (Marseille, France). Subjects were monitored prospectively and plasma ddcfDNA levels tested serially at day 15, 30, 90 and 180 post-transplant with AlleSeq cfDNA assay (CareDx), and with protocol transbronchial biopsy at day 30 and at day 15 according to the symptoms.

Results: The cohort of 45 study subjects had an average age at transplantation of 52.7 years, 55% were female and 87% received bilateral lung transplants. At day 15, all patients had a surveillance level >1%, 8/45 (18%) had biopsy proven acute rejection (AR) and 11/45 (24%) had evidence of infection (INFXN). Although at day 15 median levels of ddcfDNA in stable patients (absence of acute rejection or infection) were higher for bilateral-than for single-lung transplantation (17, 3.6% vs. 5, 1.4%, p=0.0054), the ddcfDNA decline kinetics led to no differences at day 30 (17, 1.1% vs. 5, 0.86%, p=0.2416). This initial ddcfDNA decay was yet not enough to allow lung recipients without acute rejection or infection to reach baseline levels, as 14/252 (64%) still had values >1%. At day 30, 5/45 (11%) patients had biopsy proven acute rejection and 9/45 (20%) had infection. The median ddcfDNA level for groups with acute rejection (5, 2.7%) or infection (9, 3.1%) was significantly elevated compared with the stable group (p=0.0182 and p<0.0001, respectively). At day 90 and 180, majority of subjects had surveillance ddcfDNA values <1% cut-off, and higher values were only seen in 2/45 (4%) and 8/45 (18%) of the cases, respectively.

Conclusion: We have shown that despite initial stable allograft function, a higher ddcfDNA level associates with subsequent decline of eGFR. Thus, the initial identification of subclinical graft injury could associate with long-term graft outcomes, expanding the clinical utility of dd-cfDNA.
Donor-Derived Cell-Free DNA (Dd-cfDNA) and Other Circulating Biomarkers for Assessing CAV Development in Heart Transplanted Patients

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Introduction: Cardiac Allograft Vasculopathy (CAV) is a leading cause of long-term graft dysfunction and loss after Heart Transplant (HT). The importance of the early highlight of CAV development is a marker of aggressive disease with poor clinical outcome. Despite advancements in imaging strategies, the standard for CAV assessment remains coronary angiography. Donor-derived cell free DNA (dd-cfDNA) has recently been introduced as a novel marker of graft injury in solid organ transplants. Elevations in dd-cfDNA levels may reflect new or progressive CAV development during subclinical inflammation. For this reason, dd-cfDNA could represent a non-invasive method of surveillance for CAV rejection in apparently stable post-transplant patients. Since the emerging importance of circulating biomarkers and the lack of evidences in chronic rejection of heart-transplant, we decided to evaluate the potential of dd-cfDNA in combination with other circulating molecules as alternative diagnostic biomarkers for CAV.

Materials and Methods: 31 blood samples from patients who underwent heart transplant at the ASUFC Cardiac Surgery Unit in the last 10 years, were analyzed by Next Generation Sequencing (NGS) according to CareDx Alloseq protocol. The cfDNA was extracted starting from 2mL of plasma (Qiagen). Sequencing was performed on the Illumina Miseq platform. Troponin T (TnT-hs) and NT-proBNP (Brain Natriuretic Peptide) were measured by automated immunoassay analysers. All statistics were performed by STATA software and significance was set at p < 0.05.

Results: In this study, heart transplant recipients were divided into 2 groups: 16 patients with a known CAV status while 15 patients who had not (no-CAV). A significant difference in dd-cfDNA fraction was found between CAV and no-CAV patients (p=0.03); with mean values of 0.41% e 0.13%, respectively. Neither NT-proBNP (p=0.08) nor TnT-hs (p=0.31) concentrations were found significantly different between the two groups, but a positive correlation was found between the two biomarkers (r 0.6966; p=0.0013). A trend of linear relationship emerged between cfDNA and NT-proBNP levels (r 0.4155; p=0.08).

Conclusions: With this study, we demonstrated the feasibility of evaluating dd-cfDNA in long-term heart transplanted patients and its possible association with CAV development. Further investigations are warranted to explore a possible association between dd-cfDNA levels other circulating biomarkers and CAV progression. The definition of “homogeneous” subgroups of patients basing on a “risk score” will allow to better manage their follow up and improve their prognosis.
Dynamic of Donor Derived Cell-Free DNA and Blood Gene Expression After Pancreas Transplantation

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Introduction: Donor-derived cell-free DNA (dd-cfDNA) is a noninvasive test that had demonstrated high predictive performance for acute rejection in solid organ transplant. However, combining dd-cfDNA with a gene expression profile assay could improve the diagnostic of subclinical acute rejection episodes. We aimed at evaluating the combination of these two molecular diagnostic methods in pancreas transplantation.

Materials and Methods: We conducted a prospective longitudinal study including all pancreas transplant recipients from our center from January 2017 to December 2018. Plasma samples were collected before transplant (D0), and at 1h, 24h and 7 days (D7) post-transplant, and at time of pancreas biopsy – either surveillance at 3 weeks (B3) and 12 months (B12), or per clinical indication. Biopsies were classified according to the Banff criteria. Dd-cfDNA percentage (%) was assessed using Eurofins Genoma AlloNext® by Next Generation Sequencing (NGS). Gene expression profiles, measured at the time of pancreas biopsy, were analysed with TruGraf®, a Blood Gene Expression Test of Eurofins_Transplant Genomics that uses a PCR-based assay to analyse gene expression from peripheral blood and assign a result of either “TX” (normal, no rejection) or “not-TX” (rejection).

Results: A total of 77 patients were included (SPK n=65; PAK n=12). Dd-cfDNA increased significantly at 1h and 24h after transplantation compared to baseline (D0), most likely reflecting ischemia/reperfusion damage. No correlation with either donor demographics nor cold ischemia time was identified (p>0.05). In 52 cases a biopsy-related sample was obtained (Banff criteria: No rejection n=33; Indeterminate n=5; TCMR grade 1-3 n=15; ABMR n=4). In patients with stable graft function (no rejection during the first 12months) dd-cfDNA decreased by D7 and remained low at B3 and B12 (D0 (0.27±0.14), 1h (4.30±2.53), 24h (2.41±1.79), D7 (0.65±0.47), B3 (0.47±0.28) and B12 (0.61±1.31)) Figure 1.

However, in patients with biopsy proven acute rejection (TCMR; 1.74±2.08 or ABMR; 4.42±2.93; p<0.01) % dd-cfDNA increased compared with no proven acute rejection biopsies (N-BPAR; 0.45±0.77). Furthermore, a 1% threshold had a positive predictive value to detect 86% rejection, whereas the negative predictive value was 69%. In the gene expression study 75 patients with biopsy-related sample were included: N-BPAR=41; TCMR=23; ABMR=3 and undetermined=8. The study is currently ongoing. We expect to have more conclusive data in the coming months.

Conclusion: We describe the first dd-cfDNA dynamic analysis in pancreas transplant recipients, validating its application for longitudinal monitoring in clinical practice. Combining these results with gene expression profile assay may improve the performance for the diagnosis of subclinical rejection.
Longitudinal Surveillance of a Kidney Transplant Recipient During Pregnancy Using Quantification of Fetal and Donor-derived Cell-Free DNA

Jake Miles, Vasishta Tatapudi, Apra Mattoo, Irfana Soomro, Judith Benstein, Nicole Ali

Introduction: Following kidney transplantation, women of childbearing age often experience rapid restoration of fertility as the feedback mechanisms of the hypothalamic-pituitary-gonadal axis normalize. Although rates of rejection during pregnancy are comparable to the non-pregnant transplant population, subtle indications of allograft injury such as increases in serum creatinine or proteinuria can be masked by pregnancy related changes. Here, we describe a novel approach of allograft surveillance using quantification of fetal and donor-derived cell-free DNA (dd-cfDNA) throughout gestation and postpartum.

Methods: The patient was monitored longitudinally with dd-cfDNA (AlloSure, CareDx) pre-pregnancy, during gestation and postpartum. For this analysis, specific SNPs were selected that are heterozygous in kidney donor and homozygous (same allele) in recipient and fetal cells. An average minor allele frequency (MAF) was calculated from these selected SNPs. This average represents half of the expected donor cfDNA% due to Hardy-Weinberg principle based on Mendelian genetics. Hence, calculated average MAF was multiplied by factor of 2 to calculate the kidney donor percentage.

Results: A 39 year old female with a living related kidney transplant (transplanted September 2018) conceived in February 2021. The patient had a baseline creatinine of 1.4 mg/dl and median dd-cfDNA level of 0.44%. dd-cfDNA levels remained stable throughout pregnancy (median 0.42%, IQR 0.31-0.44%) and were consistent with pre-pregnancy baseline, in keeping with absence of allograft injury. The percentage of fetal cfDNA saw an exponential rise in the first trimester, plateaued in the second trimester and showed a rapid decay post-delivery. Allograft function remained stable throughout pregnancy until development of pre-eclampsia with an acute rise in serum creatinine to 2.1 mg/dl, prompting delivery at 31 weeks (Figure 1).

Conclusions: The estimated percent of fetal fraction of cfDNA increased with gestational age and rapidly declined post-delivery. Throughout pregnancy, dd-cfDNA levels remained consistent with pre-pregnancy baseline in the absence of graft dysfunction, rejection, or clinical events. This case study suggests that longitudinal monitoring of fetal and dd-cfDNA contributions during pregnancy in kidney transplant recipients is a feasible, novel approach for allograft surveillance in this high-risk patient population.

Figure 1: Case study demonstrating the kinetics of fetal and donor-derived cell-free DNA pre-pregnancy, during gestation and postpartum (n=1). Dots represent date of conception. Dots represent individual datapoints, lines represent cubic spline curves for each variable.

Table 1: Demographics

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Kinetics of dd-cfDNA in Kidney Transplant Recipients Following SARS-CoV-2 Vaccination Booster Administration

Nicole Ali, Jake Miles, Vasishta Tatapudi, Apra Mattoo, Irfana Soomro, Judith Benstein, Sapna Mehta, Mary Neumann, Fainareti Zervou, Robert Montgomery

Introduction: Following kidney transplantation, women of childbearing age often experience rapid restoration of fertility as the feedback mechanisms of the hypothalamic-pituitary-gonadal axis normalize. Although rates of rejection during pregnancy are comparable to the non-pregnant transplant population, subtle indications of allograft injury such as increases in serum creatinine or proteinuria can be masked by pregnancy related changes. Here, we describe a novel approach of allograft surveillance using quantification of fetal and donor-derived cell-free DNA (dd-cfDNA) throughout gestation and postpartum.

Methods: The patient was monitored longitudinally with dd-cfDNA (AlloSure, CareDx) pre-pregnancy, during gestation and postpartum. For this analysis, specific SNPs were selected that are heterozygous in kidney donor and homozygous (same allele) in recipient and fetal cells. An average minor allele frequency (MAF) was calculated from these selected SNPs. This average represents half of the expected donor cfDNA% due to Hardy-Weinberg principle based on Mendelian genetics. Hence, calculated average MAF was multiplied by factor of 2 to calculate the kidney donor percentage.

Results: A 39 year old female with a living related kidney transplant (transplanted September 2018) conceived in February 2021. The patient had a baseline creatinine of 1.4 mg/dl and median dd-cfDNA level of 0.44%. dd-cfDNA levels were established a median of 9 days (IQR 2.25 – 16 days) prior to vaccination. The median level of dd-cfDNA pre-booster was 0.17% (IQR 0.12% – 0.25%). There was no significant difference in median levels of dd-cfDNA up to 30 days post-booster vaccination (Kruskal Wallis test with multiple comparisons, all p values >0.99, Figure 1). No adverse clinical events or acute rejection episodes were recorded within 30 days of SARS-CoV-2 booster administration in this cohort.

Conclusions: Median dd-cfDNA levels were not impacted by SARS-CoV-2 vaccine booster administration, suggesting that patterns of subclinical injury that may potentiate inflammation, allosensitization or allograft rejection are unlikely in this setting. The stability of dd-cfDNA demonstrated here further reinforces the safety profile of SARS-CoV-2 vaccine booster administration in KTRs.
Shedding Light on the Phenomenon of International Travel for Transplantation: The Council of Europe Network of National Focal Points

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Travel for transplantation is a complex phenomenon. Although in certain instances unethical and linked to transplant tourism, there are legitimate reasons for traveling to receive an organ transplant abroad, including family reasons, transnational co-operation agreements or access to better transplant services for related donor–recipient pairs. However, at present, very limited data is available on the international scope of the phenomenon, the profile of donors and recipients, the quality of the transfer of care, the impact on origin and destination countries, and potential risks. In 2016, the Council of Europe established the Network of National Focal Points (NFP) on Travel for Transplantation. This network is composed of reference persons, designated by countries and based at existing national transplantation organisations and/or Ministries of Health, tasked with collecting rigorous and comprehensive data on recipients and/or donors who travelled abroad in the context of a transplant procedure. They are also in charge of increasing awareness among health authorities and healthcare professionals on transplant-related crimes and developing national protocols and codes of conduct to provide an adequate framework within the medical field to prevent, detect and report transplant-related crimes, including the training of healthcare staff likely to encounter them in their professional practice. Importantly, they act as a reference person to exchange and disseminate information at national and international level on transplant-related crimes and help establish multidisciplinary synergies and a multi-agency approach to ensure an effective fight against transplant-related crimes. Currently, 35 countries have designated a NFP, including countries outside the Council of Europe borders.

In June 2017, the Registry on International Travel for Transplantation Activity (RITTA) was launched. NFP submit information annually on all patients who received an organ transplant abroad, as well as non-resident donor-recipient pairs who underwent a transplant procedure in the reporting country. Currently, RITTA includes information on 479 transplant procedures, including pseudoanonymized information about recipients, donors, transplant teams, suitability and reasons for referral for transplantation abroad, organ transplanted, status of the recipient on their home country waiting list, quality of the transfer of care, etc. Thanks to this detailed information, the network can analyse the possible legitimacy of the procedures. The international exchange of information on these patients is helping to better understand the phenomenon of travel for transplantation, assess its dimensions and identify possible hotspots of transplant tourism deserving careful investigation by the countries concerned. In addition, it is helping to gain better knowledge of the profile of donors and recipients, the quality of the transfer of recipient care and its impact on post-transplant outcomes.

EDQM/Council of Europe Network of National Focal Points on Travel for Transplantation.
Aftercare for Organ Donor Families: A Content Analysis of Organ Procurement Organization Family Services and Educational Materials

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Purpose: Following a sudden and tragic loss, organ donor families’ members experience grief, and may even develop prolonged grief disorder. All US organ procurement organizations (OPOs) provide family support and aftercare services for organ donor families, but the breadth and focus of services vary across OPOs. We assessed the scope and gaps of existing donor family services in the US and its territories.

Methods: Family service offerings were identified through each OPOs website (n = 57). We used qualitative content analysis to identify topics covered and delivery format; 11 categories were developed inductively based on common services offered by OPOs. The frequency of each service was reported and analyzed using descriptive statistics.

Results: Categories of existing donor family services and educational materials included written materials, podcasts, blogs, social media, support groups, provider referrals (referring individuals to specific counselors), on-site counseling, counseling and support services (providing websites and phone numbers to local counseling/support services), family/recipient connections, and celebratory and honorary events (Table 1). Of all services, celebratory and honorary events as well as written materials were universally provided by OPOs (100%). Quilts made in honor of donors were commonly provided by OPOs. The changes introduced in Portuguese criminal law for the criminalisation of organ trafficking, including the options made with respect to donors and recipients regarding their criminalisation or not, and the solutions adopted to ensure that acts committed outside the country by nationals or residents can also be punished. Secondly, we present a protocol/code of conduct to provide an appropriate framework to prevent and address transplant-related crimes for healthcare professionals. Such protocol provide guidelines for the management of patients, including on how to ensure traceability and bio-vigilance for patients who travel for transplantation, and indicators for the identification of signs of organ trafficking and/or human trafficking for the purpose of organ removal. Third, we introduce the Portuguese reporting mechanism for the communication of information about such cases to law enforcement authorities for the purposes of criminal investigation. Finally, we present the amendments made to the Medical Code of Ethics to address doctors’ concerns regarding medical confidentiality.

Conclusion: Counseling and support services for organ donor families vary by OPO and can be improved. The development and implementation of evidence-based grief programs tailored to these families can improve quality of services to support donor families.

<table>
<thead>
<tr>
<th>Donor Family Service</th>
<th>Frequency distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Written materials</td>
<td>100.00% (n = 57)</td>
</tr>
<tr>
<td>Celebratory and honorary events</td>
<td>100.00% (57)</td>
</tr>
<tr>
<td>Family/Recipient connection</td>
<td>98.25% (56)</td>
</tr>
<tr>
<td>Counseling Recommendations</td>
<td>85.96% (49)</td>
</tr>
<tr>
<td>Social media</td>
<td>47.37% (27)</td>
</tr>
<tr>
<td>Blogs</td>
<td>38.60% (22)</td>
</tr>
<tr>
<td>Videos</td>
<td>35.09% (20)</td>
</tr>
<tr>
<td>Podcasts</td>
<td>33.33% (19)</td>
</tr>
<tr>
<td>Provider referrals</td>
<td>15.79% (9)</td>
</tr>
<tr>
<td>Support groups</td>
<td>14.04% (8)</td>
</tr>
<tr>
<td>On-site counseling</td>
<td>8.77% (5)</td>
</tr>
</tbody>
</table>
Kidney Transplant in Mentally Challenged Patients: A Single Centre Experience

Jude Yagan1, Tarek Mahmoud1, Osama Geith1, Omar AlKandari1, Nabil ElSerwey2, Mohamad Enam1, Prasad Nair1, Torki AlOtaibi1.
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Introduction: Kidney transplant is the best choice of treatment for patients with end stage kidney disease. Some medical conditions that can pose an ethical and legal questions on kidney allocation, like the psychological and mental status of the recipient. Children with severe neurological dysfunciton without any anticipated improvement, can create an ethical dilemma on whether to allocate them a deceased donor kidney transplant knowing the quality of life of deceased compared with their peers. On the other hand there is an ethical obligation to provide the best of care for this vulnerable group.

Methods: We retrospectively studied children with Kidney transplant (KTx) in organ transplant center in Kuwait. Children have a background diagnosis of mental retardation with variable severity ranging from mild to severe, most of the children have urological developmental abnormalities as the cause of end stage kidney disease (ESKD). We included all types of donors, that is live related (LRKTx), live unrelated (LUKTx) and deceased donor (DDKTx). Nine of the children were without a labeled diagnosis (global developmental delay, cerebral palsy) one has Jeune syndrome with mild cognition dysfunction (received a combined deceased donor liver and kidney transplant); one has Laurence-moon-Biedl syndrome, and one Down syndrome received LUKTx. We briefly interviewed the families during their scheduled outpatient visit asking questions about improved quality of life, mainly: social and emotional well-being.

Results: Ten (10) children fulfilled the above criteria were followed up for up to 23 years (the oldest surviving transplant with these criteria in our center) with a mean age at transplant time of 7.8 years. Four (4) (LRKTx), similar number (4) from (DDKTx) and two (2) were (LUKTx). The mean serum creatinine of 135umol/l upon last follow up. Families of the children were interviewed to discuss the impact of kidney transplant on their life: relieve the families from the burden of maintenance HD or PD and provide better quality of life to the children. The general misconception about inabilities to follow complex medication regimen and nonadherence in this group of mentally challenged patients is highly challenged in this cohort, with good support from our center with follow up and medical education. There were no rejection episodes and no prolonged hospitalization episodes except for mild infections (UTIs, chest infection).

Conclusion: Mentally challenged individuals should not be denied a chance for kidney transplant based only on their mental condition. Issues of nonadherence can be overcome with stable family support even in patients with devastating neurological dysfunction. It gave the families a better quality of life and relief the ethical issues surrounding depriving this group from the best care while insuring no waste of precious organ.

Grant Funding to Support Increased Access to Transplant Care for Patients and Caregivers

Talia Giordano1, Jan L Weinstock Esq.1,2
1Caregiver Lifeline Program, Gift of Life Family House, Philadelphia, PA, United States; 2Administration, Gift of Life Donor Program, Philadelphia, PA, United States.

Introduction: Patients experiencing end-stage organ failure face many challenges that can result in financial distress for the patient and caregiver. Financial distress can limit access to transplant care, which has become an increasing concern as the transplant list continues to grow and disparities in access are highlighted. Our region’s Organ Procurement Organization (OPO)’s affiliated transplant hospitality house supports the lodging, transportation and support needs of patients traveling into one city for treatment at its 7 city transplant centers. The remaining transplant Regional Centers (RC) in the OPO region are located outside of the city in areas not supported by the hospitality house. Interviews with RCs highlighted that RCs’ transplant patients needed assistance for travel and lodging to support access to transplant care.

Method: The OPO affiliated Foundation established The Transplant Center Family Support Grant Program through which 9 RCs can apply for up to $25,000 a year to support their patients’ travel, lodging and food needs related to their transplant care. Each RC application was vetted and approved based on the grant guidelines. Approved applicants were required to implement systems for releasing and tracking disbursed funds and submit quarterly logs with de-identified information on utilization.

Results: Between 2019-2021, 9 hospitals received a total of $313,371. Grant funds were distributed to 1,947 non-unique, patient/caregiver units (Pt/CGs), totaling $236,636 in utilization and an average of $121 per distribution. Of the $236,636, $135,736 (57%) was utilized for transportation support, $82,126(35%) was utilized for lodging support, $18,237(8%) was utilized for food support, and the remaining was other.

Of the 1,947 Pt/CGs receiving funds, 1,517 were to kidney Pt/CGs(78%), 279 were for liver Pt/CGs(14%), and 75 were for heart Pt/CGs(4%). The primary reason for the Pt/CG support was as follows: 591(30%) were for Pt/CGs evaluation to be listed and 569(29%) for post-transplant appointments. Pt/CGs utilizing funds for transplant surgery was 289(15%) and the remaining(less than 10%) for each pre-transplant appointment (once listed), hospitalization (not for transplant surgery), or left blank. Based on the 3-year data, transportation support was the most significant need for Pt/CGs. Similarly, kidney Pt/CGs presented most frequently with the largest need to facilitate evaluation and post-transplant appointments.

Conclusion: The Regional Centers Grant Program is just one example of a program that may enhance access to care, especially for Pt/CGs with limited means and difficulty accessing transportation, lodging and food. Further examination should be done of this program and other innovative programs to support access to care, particularly for those facing financial and other barriers to determine impact and effectiveness and promote equity in transplant care.
Fatigue and Resilience in Organ and Tissue Transplant Patients Facing the Pandemic of COVID-19

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Background/Aims: For organ and tissue transplant recipients, the pandemic of COVID-19 caused several uncertainties, especially the fear of contagion, which may have been one of the stressors. On the other hand, when facing this adversity situation, some transplant recipients, overcome it beneficially, performing their resilience. The objective of this study is to analyze the fatigue and resilience of organ and tissue transplant recipients in the pandemic of COVID-19 in Brazil.

Methodology: Cross-sectional study, carried out with organ and tissue transplanted patients in Brazil. The inclusion criteria were: patients who performed organ and tissue transplantation at least three months ago in the pandemic. Data collection occurred through disclosure in social networks and web pages between January and April 2021, with the instruments: sociodemographic and clinical data questionnaire, Wagnild and Yong’s resilience scale and the pictogram of fatigue. The data were organized after importing Microsoft Excel spreadsheets from REDCap. The analysis was performed using descriptive and inferential statistics, adopting statistical significance of p<0.05. The study was approved by an institutional ethics committee and complies with national and international guidelines for research with human beings.

Results: 548 organ and tissue transplant recipients participated in the study. The mean age of transplant recipients was 45.58 years (SD: 6.40), 325 (59.31%) were mostly female, 318 (58.03%) were white, 280 had completed higher education (51.57%) and from the Southeast region 338 (61.68%). The mean time of transplantation was 6.95 years (SD: 6.83) and the occurrence of fatigue was 4.27 months (SD: 12.05). The rinse transplants 320 (58.39%), liver 131 (23.91%), heart 27 (4.93%) and cornea 21 (3.83%) stand out. Flexibility transplants were more resilient and corneal transplants were more fatigued. Individuals who perform informal work and had no other symptoms were more resilient (p=0.022, p<0.001, respectively). Females had their fatigue intensity classified as "moderately tired" (p<0.001) and those with a partner as "a little tired" (p=0.021).

Conclusion: The stressors arising from the pandemic moment may have led to an increase in fatigue and moderate performance of resilience in organ and tissue transplant patients, which indicates a need for health professionals to support and carry out stimulus programs to increase resilience and fatigue reduction. We thank all the transplant recipients who took the time to answer the survey. This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001.
International Travel for Organ Transplantation: Challenges in Registry Data Collection?

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Introduction: International travel for organ transplantation (ITOT) may involve ethically legitimate transplants as well as organ trafficking or transplantation that undermines self-sufficiency in destination countries (“transplant tourism”). The proportion of worldwide solid organ transplants suspected to involve organ trafficking or transplant tourism, is regularly cited as 5-10%. However, this figure is more a rule of thumb than an evidence-based estimate. There are also limited data about ITOT in general, including data about ethically appropriate activities.

Method: Drawing on the peer reviewed literature, the aim of this study is to explore the range of current mechanisms used to collect and report data about ITOT. We examined current examples of donation and transplantation registries at national, regional and global levels. We discuss the strengths and limitations of each approach, as well as potential barriers to routine reporting to enable better quantification of ITOT.

Results: Review of the literature has demonstrated there are several factors that undermine efforts to quantify ITOT and organ trafficking even at the country level. The most important of these may be the obscuration of trafficking activities under cover of legally authorised transplants approved by ethics committees. Although there are also barriers to collection and reporting of data about legitimate ITOT, these data are increasingly available in national and international transplant registries. However, the analysis and comparison of data from different registries may be difficult in the absence of harmonization.

Conclusion: Systematic data collection and reporting of ITOT are essential for efforts to address organ trafficking, support self-sufficiency and to assist patients seeking care abroad. Mechanisms to facilitate reporting and harmonization of registry data are urgently needed.

Cost-Effectiveness of Using a Kidney Anastomosis Facilitation and Cooling Device to Eliminate Second Warm Ischemia Time

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1Department of Surgery, UCSF, San Francisco, CA, United States; 2Biosign, Stanford University, Palo Alto, CA, United States.

Introduction: The warming of a donor kidney during the vascular anastomosis of a transplant i.e., second warm-ischemia time (SWIT), is independently associated with higher rates of delayed graft function, premature graft failure, and the discard of high-risk kidneys. Existing literature shows that shortened SWIT and intra-operative cooling of a renal allograft during SWIT cumulatively reduces the incidence of delayed graft function in deceased donor kidney transplant recipients from a baseline rate of 35% to 25%, 5-year graft loss from 23% to 16%, and increases the number of transplantable kidneys by reducing the cumulative (first plus second) warm ischemia time in deceased after circulatory death (DCD) donor kidneys. Cost effectiveness of a breakthrough anastomosis facilitation and SWIT eliminating cooling device was evaluated with a Markov Model.

Methods: A state-transition model was used to predict the effect of intra-operative cooling and standard of care on 1-year and lifetime probabilities of having a functioning graft, delayed graft function, graft loss with return to dialysis, and death. We adopted a societal perspective and estimated an incremental-cost-effectiveness ratio in U.S. dollars per quality adjusted life year (QALY).

Results: Intra-operative allograft cooling of deceased donor kidneys provides a 0.01 QALY improvement and $4,800 in savings per patient at 1-year, and over a lifetime, provides 0.26 QALYs and $12,200 in savings per patient. In both the 1-year and lifetime estimates, the ICER is dominant with the cooling device. The total cost savings, not including QALY gains to the system in this group, is $228 million. Including cost savings of the projected increase in organ utilization validated via a surgeon survey (n=175) resulted in $1.18 billion in savings over the lifetime of an annual cohort of transplant recipients. The 95% credible interval for ICER was cost-saving to $39,000 per quality adjusted life year.

Conclusion: The model suggests that intra-operative cooling of a deceased donor renal allograft, over a wide range of assumptions, is a cost effective strategy for transplantation that would result in significant cost savings and lower morbidity and mortality. Use of a breakthrough designated device to eliminate intra-operative warming over a 60 minute period and thereby reduce rates of delayed graft function, increase organ longevity, and change organ acceptance practices would lead to significant cost savings.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Source</th>
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<tbody>
<tr>
<td>Cost of QALY</td>
<td>$4,800</td>
<td>Sussel et al 2020</td>
</tr>
<tr>
<td>Cost of DGF</td>
<td>$228 million</td>
<td>Sussel et al 2020</td>
</tr>
<tr>
<td>Cost of Delayed Graft Function</td>
<td>$1.18 billion</td>
<td>Sussel et al 2020</td>
</tr>
<tr>
<td>Cost of QALY with Cooling</td>
<td>$12,200</td>
<td>Sussel et al 2020</td>
</tr>
<tr>
<td>Cost of QALY without Cooling</td>
<td>$1.17 billion</td>
<td>Sussel et al 2020</td>
</tr>
<tr>
<td>Cost of Cooling Device</td>
<td>$1,000</td>
<td>Willingness to pay assumption</td>
</tr>
</tbody>
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Byers Center for Biodesign, Stanford University.

The Sun Is Still Shining: Nature of Industry Payments to Transplant Surgeons From 2014-2019

Conner Lombardi¹, Jacob Lang¹, Deklin Clayton², Puneet Sindhwani¹,³, Obi Ekwenna¹,³.
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Introduction: This study aims to characterize the nature of these payments made to transplant surgeons over the past six years of Open Payments Program (OPP) data, to better understand the nature of physician-industry relationships within transplant surgery.

Methods: The study sample included all physicians (categorized under Urology, Surgery, Pediatric Urology, and Pediatric Surgery) who received at least one non-research payment as transplant surgeons to the OPP. To capture transplant surgeons who may be listed under their pipeline specialty, the American Society of Transplant Surgeons member directory as of January 2021 was queried. Physicians identified as residents in the ASTS member directory were excluded from analysis. Data was analyzed between 2014 and 2019.

Results: Total number of transplant surgeons receiving payment 1335. Total amount in dollars paid, $15,661,536. The mean payment was $416.58 (SD $1684.60) and the median payment was $50.00 (IQR $17.44-$151.0). The top three categories include $3,910,288 (26.2%) paid for consulting fees, $4,668,147 (31.3%) paid for non-consulting fees (speaker and vendor fees), and $3,035,045 (20.3%) paid for travel and lodging. OPTN Region 5 received the most payment at 19.3%, and Region 1 received the least payment at 1.5%. The top five companies making payments include Intuitive Surgical Inc, Gilead, Norvartis, Astellas, Genzyme.

Conclusions: There is a considerable financial relationship between medical device and pharmaceutical manufacturers and transplant surgeons. The majority of non-research payments to transplant surgeons by industry sponsors were for non-consulting services. There exist regional differences in the amount paid by industry to transplant surgeons in regards to median and total industry payment amounts.
Inequitable Access to Transplants: Adults With Impaired Decision-Making Capacity

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“Ethical and Legal Issues” working group of the European Society of Transplantation

In recent years inequitable access to deceased donor organs for transplantation has received considerable scrutiny. Emerging evidence suggests that patients with impaired decision-making capacity face inequitable access to transplantation. The “Ethical and Legal Issues” working group of the European Society of Transplantation undertook an expert consensus process. Literature relating to transplantation in patients with impaired decision-making capacity was examined and collated to investigate whether impaired decision-making capacity is associated with inferior transplant outcomes and the legitimacy of this healthcare inequality was examined. Even though the available evidence of inferior transplant outcomes in these patients is limited, the working group concluded that access to transplantation in patients with impaired decision-making capacity may be inequitable. Consequently, we argue that impaired decision-making capacity should not in and of itself be considered as a barrier to either registration on the transplant waiting list or allocation of an organ. Strategies for non-discrimination should focus on ensuring that eligibility is based upon sound evidence and outcomes without reference to non-medical criteria. Recommendations to support policy makers and healthcare providers to reduce unintended inequity and inadvertent discrimination will be presented. We call upon transplant centres and national bodies to include data on decision-making capacity in routine reporting schedules in order to improve the evidence base upon which organ policy decisions are made going forward.

We thank the European Society for Organ Transplantation for facilitating the consensus process.

Attitudes and Behaviors Towards Ethical Dilemmas in Organ Transplantation and Organ Donation

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Introduction: Despite the increasing number of transplantable organs and tissues and advances in transplantation, there is a serious shortage of organ donors. Traditions, perceptions, attitudes, habits, value judgments and belief systems related to ethical dilemmas play an active role, in shortage of organ donors. The aim of this study is to evaluate the attitudes and behaviors related to these ethical dilemmas.

Method: In the cross-sectional survey study, 563 people (278 male, 285 female) evaluated 10 questions about 10 ethical aspects of organ transplantation. Participants are those working in the field of law (n=30), education (n=36), health (n=124), social services (n=50), communication (n=37), members of non-governmental organizations (n=37), people who have received Islamic education (n=23), the public (young, adult, old, n=156), individuals from different religions (n=523 Islamic, n=40 other religions) and belief groups, and people with disabilities (n=30). The ethical dimensions addressed in questions are as follows; Ethical issues in animal tissue and organ transplantation, the ethical dimension of the effect of religious belief in organ transplantation, the ethical dimension of organ transplantation within the framework of human rights, ethical problems arising from the patient-physician relationship in organ transplantation, social risk sharing and ethical dimensions in organ transplantation, the effect of organ transplantation and the role of the media in ethics, ethical problems arising from lack of informed consent in organ transplantation, ethical dilemmas in organ and tissue distribution, ethical problems in artificial tissue and organ transplantation.

Results: The mean age of participants is 36.6 ±13.9. The education level of 63.4% is at the undergraduate level. 95.7% of the participants accept organ donation from another religion. 74% accept tissue and organ transplantation from animals. 21% of the participants do not want to donate their organs in line with their religious beliefs in order to preserve their body integrity after death. 59% stated that they may be affected by the activities of political parties for organ donation. The rate of those who think that the demographic characteristics of the people waiting on the organ list should be taken into consideration is 21%. The percentage of those who stated that they would accept to receive an organ from the organ mafia if they were left in a desperate situation is 27%, and the percentage of those who are undecided is 20%. 53% of them stated that they would be highly impressed by their doctor about organ donation. Disabled participants were the most affected by their physicians’ views on organ transplantation. Cadavers were the most requested donor group if they had the right to select from the organ donor list.

Conclusion: In ethical terms, it has been determined that there are important dilemmas regarding organ transplantation in the value judgments of individuals.
Commercial Kidney Transplantation: Sociodemographic and Clinical Characteristics

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Background: Transplantation is the renal replacement therapy of choice for patients with end-stage kidney disease. In addition to the survival benefit and better quality of life, it confers an economic advantage to the health care system. Although condemned by the international community, transplant tourism and commercial transplantation are still evident. The disparity between organ supply and demand finds an outlet whenever the regulations are less strict.

Objectives: To describe the sociodemographic and clinical characteristics of patients who received a commercial transplant and address the causes to seek commercial transplantation.

Methods: A questionnaire-based survey was done from September 2021 to December 2021 at the outpatient clinic of the Nephrology and Renal Transplantation Center, Baghdad, Iraq. In Iraq, renal transplantation is a live donor, blood group compatible program. A central team should approve all donors to ascertain noncommercial conduct. As per Iraqi legislation, renal transplantation services and maintenance immunosuppression are provided free of charge at governmental hospitals. Commercial transplantation is defined as the state of paying a donor at a non-governmental unit. The questionnaire included 15 questions distributed to patients who received transplants at non-governmental units inside Iraq or sought a transplant outside the country. It provided demographic and clinical data and assessed the reason for performing a paid donation. Laboratory data were retrieved from patients records.

Results: Seventy-eight patients accepted to participate in the study. The majority (86/85%) were male, and the study group’s mean age was (43.3 ± 10.8 years). Fifty-four (69.2%) patients were below the college education level, and 47% were unemployed. The cause for ESRD was unknown in 51%. All donors were live unrelated, and five patients (6.41%) had their transplants outside Iraq. The duration of the hospital stay was 5-14 days. The time since transplantation was 1 to 5 years.

The reported complications at 1-year post-transplantation were: rejection (15%), wound infection (2.5%), CMV infection (1%), and recurrent disease (1%). The mean serum creatinine at one year was 1.27 ± 0.52 mg/dl. At five years, 14 patients (17.94%) had a diagnosis of chronic allograft dysfunction. The leading reason for seeking commercial transplantation was the unavailability of the biologically related or unrelated altruistic donor in 74% of the study participants. In 2008 our program performed one third of the overall PT of the country and in 2020, 59% of overall national PT. As our mean waiting time for SPK has been about 2 years, we have encouraged patients to living-kidney donation, allowing living-kidney transplant first followed by PAK or simultaneous pancreas and living-donor kidney transplants. Our immunosuppression protocol has evolved from induction with OKT3 to a non-induction protocol in SPKs and then to depleting induction with thymoglobulin for all PT and maintenance with tacrolimus, mycophenolate mofetil or sodic and steroids. Surgical techniques were initially systemic-bladder, progressing to systemic-enteric(dudenojejunostomy), then portal-enteric, portal duodenal and more recently systemic(cava)-duodenal drainage. Postoperative management has also improved and based on early discharge(between 5-7 days hospital stay) and a day-clinic basis follow-up, completing the remainder

Annual Number of PT- HEPATO
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Over 1,000 Pancreas Transplantation in a Latin American Program

Marcelo Pereira1, Juan Branez1, Fernanda Danziere1, Leonardo T. Mota1, Beimar Zevallos1, Marcio Paredes1, Aline R. Magalhães1, Leon Alvim1, Ana Claudia Vidal1, Celia Watanabe1, Tércio Genzini1
1Department of Abdominal Organ Transplantation, Leforte Hospital, São Paulo, Brazil.

Introduction: There has been a worldwide tendency of decline in the annual number of pancreas transplants(PT). The maintenance of high-volume PT programs is of major importance both for assistance goals as for teaching new generation of PT surgeons and clinicians. We aim to present the lessons learned from over 1,000 PT in a Brazilian program.

Methods: We analyzed a 25-year period according to PT activity, immunosuppression, surgical techniques, postoperative management and outcomes.

Results: Overall, 1,081 PT were analyzed, being 601 SPK and 480 solitary PT, out of which 331 PAK and 149 PTA. We have maintained a high-volume activity over these 25 years, highlighting the growing of the program in more recent years(Figure). Over half of our pancreatic donor are procured outside of our regional and very frequently we procure donors in distant states of the country. Since 2014, pancreas allocation has been based on virtual cross-match which has significantly reduced our mean ischemia time for approximately 8hours. In 2008 our program performed one third of the overall PT of the country and in 2020, 59% of overall national PT. As our mean waiting time for SPK has been about 2 years, we have encouraged patients to living-kidney donation, allowing living-kidney transplant first followed by PAK or simultaneous pancreas and living-donor kidney transplants. Our immunosuppression protocol has evolved from induction with OKT3 to a non-induction protocol in SPKs and then to depleting induction with thymoglobulin for all PT and maintenance with tacrolimus, mycophenolate mofetil or sodic and steroids. Surgical techniques were initially systemic-bladder, progressing to systemic-enteric(dudenojejunostomy), then portal-enteric, portal duodenal and more recently systemic(cava)-duodenal drainage. Postoperative management has also improved and based on early discharge(between 5-7 days hospital stay) and a day-clinic basis follow-up, completing the remaining

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Ipsilateral Simultaneous Pancreas-Kidney Transplantation With Concomitant Reperfusion of Both Grafts Versus Contralateral SPK Transplantation: A Single-Center Analysis of 168 Cases

Marcelo Pereira1, Juan Banean2, Fernanda Danderleire3, Aline M. Rocha1, Adriana B. Bortoluzzo2, Maria K. Venezuela2, Ana C. Vidigal1.

1Department of Abdominal Organ Transplantation, Leforte Hospital, São Paulo, Brazil; 2Statistics and Data Science, Brazil, INSPE, Institute of Education and Research, São Paulo, Brazil.

Introduction: Ipsilateral simultaneous pancreas-kidney transplantation (SPK) is an attractive surgical strategy searching to reduce operative time and preserve the left iliac fossa for an eventual future transplant. Traditionally, pancreas is placed and reperfused first followed by kidney transplant. The aim of the study was to compare a technical variant of iSPK (v-iSPK) with concomitant reperfusion of both pancreas and kidney grafts to the standard contralateral SPK (cSPK).

Methods: A retrospective analysis was performed of 42 v-iSPK and 117 cSPK from 2018 to 2022. There was also a small group (n=9) of iSPK without concomitant reperfusion (iSPKw/o) for comparison of some specific variables. The decision for graft placement was made during the procedure and based on physical characteristics both of recipient (dimension of pelvis, quality of vessels) and of donor pancreas and kidney. In v-iSPK pancreas was firstly reperfused and after a few minutes for homostasis, kidney was soon reperfused. Donor and recipient data, surgical and cold ischemia time (CIT), delta time between kidney and pancreas CIT, surgical complications, reoperations and patient and graft survival were compared between the 2 groups.

Results: Donor age (28.5 ± 28.3) and KDPI (26.2 ± 23.8), recipient age (36.5 ± 35.8), race and gender were similar between v-iSPK and cSPK, respectively. Cerebrovascular event as cause of donor death (33.3% x 25.6%, p=0.46) and rate of preemptive SPK (4.8% x 2.6%, p=0.85) were also similar between v-iSPK and cSPK groups. The operative time was shorter (312 x 329 min, p=0.05) while pancreas CIT was higher (8.7 ± 7.8 hours, p<0.001) and kidney CIT was lower (8.8 ± 9.9 hours, p<0.001) for v-iSPK. Delta time between kidney and pancreas CIT, surgical complications, reoperations and patient and graft survival were similar between the 2 groups.

Conclusion: v-iSPK is a new variant technique and seems to be as safe as the standard cSPK. The attractive of this new technique is to facilitate the implantation of the ipsilateral kidney graft with a still empty pancreas graft and can shorten surgical time and the time-interval between pancreas and kidney reperfusion in addition to reduce pancreas technical failure.
234.4
Survival After Simultaneous Pancreas-Kidney Transplantation in Type 1 Diabetes: The Critical Role of Early Pancreas Allograft Function

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1Washington University School of Medicine at St. Louis, St. Louis, MO, United States; 2Saint Louis University, Saint Louis, MO, United States; 3Emory University, Atlanta, GA, United States.

Objective: Simultaneous pancreas-kidney transplantation (SPK) is a well-established treatment option for patients with diabetes mellitus and end-stage kidney disease, but SPK carries a 7-22% rate of technical failure. The impact of early pancreas graft function on subsequent kidney graft and patient survival in type 1 diabetic recipients of SPK is not well-defined.

Methods: We examined national U.S. transplant registry data for type 1 diabetic patients who received SPK between 2000 and 2021 and survived the first 3 months with a functioning kidney. Transplant patients were categorized as: deceased-donor kidney transplant alone (DDKA), living-donor kidney transplant alone (LDKA), SPK recipients with a functioning pancreas graft 3 months posttransplant (SPK,P+), or SPK recipients with pancreas graft failure within 3 months posttransplant (SPK,P-). Associations of transplant type with kidney graft failure and patient survival through September 2021 were estimated by multivariable inverse probability of treatment weighted (IPTW) accelerated failure-time (AFT) models, with weights estimated using generalized boosted regression.

Results: Compared to SPK,P+ recipients, LDKA had 18% less graft survival time (TR: 0.730.820.92) and 18% less patient survival time (TR: 0.720.820.93), DDKA had 23% less graft survival time (TR: 0.710.770.85) and 29% less patient survival time (TR: 0.640.710.79), and SPK,P- had 34% less graft survival time (TR: 0.590.660.75) and 34% less patient survival time (TR: 0.580.660.75). Compared to LDKA, SPK,P- had 19% less graft survival time (TR: 0.700.810.94) and 19% less graft survival time (TR: 0.690.810.95). Compared to DDKA recipients, SPK,P- had 14% less graft survival time (TR: 0.760.860.97). No difference was found for patient survival time between SPK,P- and DDKA.

Conclusions: SPK recipients with functioning pancreas grafts within 3-month posttransplant have better kidney allograft and patient survival compared with LDKA and DDKA. Early pancreas graft failure results in inferior kidney and patient survival time compared to kidney transplant alone.

This study was supported by grant 4746 from the Foundation for Barnes-Jewish Hospital.

Table 1: Model Results of Multivariable Inverse Probability of Treatment Weighted (IPTW) Weibull Accelerated Failure-time (AFT) for Graft Failure and Patient Death

<table>
<thead>
<tr>
<th>Event</th>
<th>Kidney graft failure</th>
<th>Patient death</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPK,P+</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>LDKA</td>
<td>0.82 (0.73, 0.92)**</td>
<td>0.82 (0.72, 0.93)**</td>
</tr>
<tr>
<td>DDKA</td>
<td>0.77 (0.71, 0.83)**</td>
<td>0.71 (0.64, 0.79)**</td>
</tr>
<tr>
<td>SPK,P-</td>
<td>0.66 (0.59, 0.75)**</td>
<td>0.66 (0.58, 0.75)**</td>
</tr>
</tbody>
</table>

Note: Multivariable analysis was adjusted for recipients’ factors (age, gender, race, BMI, diabetes status, donor-recipient cytogenetic risk status), donor factors (age, gender, race, BMI, hypertension status), and transplant factors (cold ischemia time, human leukocyte antigen mismatch). *p<0.05; **p<0.01; ***p<0.001
Portal-Endocrine and Gastric-Exocrine Drainage Technique in Pancreas Transplantation

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Background: Diagnosis of rejection has continued to be problematic in pancreas transplantation (PT). In 2007, we innovated a new surgical technique for PT, portal-endocrine and gastric exocrine drainage (P-G) technique, where the end of allograft jejunum was anastomosed to the anterior aspect of the stomach, facilitating endoscopic access to duodenum/pancreas allograft.

Objective: The aim of our study was to evaluate the safety, measure allograft rejection, and calculate graft and patient survival in patients who underwent PT with the P-G technique.

Method: This was a retrospective review study of 127 PT patients with the P-G technique from Sep 2007 to Dec 2021 at our center. 113 simultaneous kidney-pancreas transplants (SKPT), 10 pancreas-alone transplants, and 4 pancreas-after-kidney transplants were performed. Baseline demographics, OR time, estimated blood loss (EBL), cold ischemic time (CIT) for kidney and pancreas allografts, length of hospital stay (LOS), complications, number of patients with endoscopy, number of patients with allograft rejection, death-censored 5-year kidney and pancreas graft survival, and 5-year patient survival were calculated.

Results: Table 1 summarizes baseline demographics and Table 2 highlights complications and outcomes. Perioperative complications included 8 post-operative bleeds and 7 vascular thromboses. Patients with vascular thrombosis had subsequent transplant pancreatectomies within 6 weeks. During the study period, 51 transplant patients underwent upper GI endoscopy. Duodenum/pancreas allograft rejection was found in 28 patients. The death-censored 5-year graft survival for pancreas and kidney were 83.5 % and 84.6 %, respectively. Patient survival was 87.4%. Figure 1 shows the Kaplan-Meier curves for pancreas graft, kidney graft, and patient survival.

Conclusion: This P-G drainage technique for PT has proven to be safe with comparable graft and patient outcomes. Access to donor duodenum and pancreas allograft via endoscopy is unique to this technique and provides the added advantage of life-long easy access to the allograft.

<table>
<thead>
<tr>
<th>Pancreas Transplants (n=127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKPT, % (n)</td>
</tr>
<tr>
<td>Pancreas-alone transplants, % (n)</td>
</tr>
<tr>
<td>Pancreas-after-kidney transplants, % (n)</td>
</tr>
<tr>
<td>Age (yr), mean ± SD</td>
</tr>
<tr>
<td>Gender, % (n)</td>
</tr>
<tr>
<td>Male: 57.5 (71); Female: 42.5 (54)</td>
</tr>
<tr>
<td>Race, % (n)</td>
</tr>
<tr>
<td>Caucasian: 48.0 (61); African-American: 48.0 (61); Hispanic: 3.9 (5)</td>
</tr>
<tr>
<td>BMI pre-transplanted (kg/m²), mean ± SD</td>
</tr>
<tr>
<td>Type of OPA, % (n)</td>
</tr>
<tr>
<td>Type 1 OPA: 70.9 (90); Type 2 OPA: 29.1 (37)</td>
</tr>
<tr>
<td>Duration of OPA (min), mean ± SD</td>
</tr>
<tr>
<td>OR time (h:mn), mean ± SD</td>
</tr>
<tr>
<td>EBL (ml), mean ± SD</td>
</tr>
<tr>
<td>CIT Pancreas (h:mn), mean ± SD</td>
</tr>
<tr>
<td>CIT Kidney (h:mn), mean ± SD</td>
</tr>
<tr>
<td>LOS (days), mean ± SD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pancreas Transplants (n=127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-operative bleeding, % (n)</td>
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<tr>
<td>Vascular Thrombosis, % (n)</td>
</tr>
<tr>
<td>Wound Dehiscence, % (n)</td>
</tr>
<tr>
<td>Surgical Site Infection, % (n)</td>
</tr>
<tr>
<td>Perinephric fluid collection, % (n)</td>
</tr>
<tr>
<td>Bowel Perforation, % (n)</td>
</tr>
<tr>
<td>Number of patients with endoscopy, % (n)</td>
</tr>
<tr>
<td>Number of patients with duodenal/pancreas allograft rejection, % (n)</td>
</tr>
<tr>
<td>Number of patients with duodenum allograft rejection, % (n/total)</td>
</tr>
<tr>
<td>Number of patients with pancreas allograft rejection, % (n/total)</td>
</tr>
<tr>
<td>Number of patients with kidney allograft rejection, % (n/total)</td>
</tr>
<tr>
<td>Pancreas 5-year graft survival, % (n)</td>
</tr>
<tr>
<td>Kidney 5-year graft survival, % (n/total)</td>
</tr>
<tr>
<td>Patient 5-year survival, % (n)</td>
</tr>
</tbody>
</table>
Pancreas Graft Rejection: Incidence, Treatment and Outcomes

Pablo Uva, 1,2,3,Alejandra Quevedo, 1, Josefina Roses1, Roxana Pilotti1, Maria F Toniolo1, Esteban Alvarez,3, Eduardo Chuluyan2.
1Pancreas Transplantation, Instituto de Transplantes y Alta Complejidad (ITAC-Nephrology), Buenos Aires, Argentina; 2Pancreas Transplantation, Hospital General de Agudos “Dr. Cosme Argerich”, Buenos Aires, Argentina; 3CEFyBO, CONICET, Buenos Aires, Argentina.

Introduction: Pancreas rejection continues to be a major cause of graft failure (GF). Treatment protocols differ among transplant centers.

Materials and Methods: Since December 2011 pancreas biopsies are performed systematically at any graft dysfunction and pancreas rejection is treated according to rejection type and grade. The objective is to report incidence, type, grade, treatment and outcomes of pancreas rejection until March, 2022. Standard anti-rejection treatment: Indeterminate and Banff 1: Steroid pulses, Banff 2: SP+ Thymoglobulin. AMR: Steroid pulses, plasmapheresis and Mx, Mixed rejection: SP+Thymo+PP+IVG. However, due to kidney discordant grade or rejection and/or patient condition, treatment may have varied.

Results: We have performed 419 pancreas transplants at our center, of which 242 were performed during the study period. The incidence of rejection was 17% at 1y and 25% at 5y. We analyzed 93 pancreas biopsy proven rejections. Among the 71 first episodes, there were 4 indeterminate rejections (0% GF), 43 Banff 1 rejections (7% GF), 15 Banff 2 rejections (33% GF) and 4 AMR (20% GF) and 1 chronic rejection (100% GF). Recurrence of rejection after a first episode was 11% for Banff 1 and 50% for Banff 2 and AMR cases. Among the 22 episodes of recurrent rejection there were 1 indeterminate rejection (0% GF), 14 Banff 1 rejection (7% GF), 4 Banff 2 (0 % GF), 2 AMR (100% GF) and 1 chronic rejection (100% GF). In 29 cases, a repeat biopsy was performed during the first 2 months after initial treatment confirming persistent rejection (12), resolution of rejection (16 cases) or graft failure (1 case).

Discussion: Pancreas rejection is still a prevalent complication after transplantation. Tailoring anti-rejection treatment according to pancreas pathology, kidney pathology and patient status may result in a more efficient use of immunosuppression. Repeat biopsy can assist differentiate cases or persistent rejection vs resolution of rejection when elevated enzymes or hyperglycemia persists after treatment.

Table 1: Treatment and outcomes according to rejection type and grade for first episode of rejection cases

<table>
<thead>
<tr>
<th>Rejection Type</th>
<th>No.</th>
<th>Initial Episode</th>
<th>2nd Episode</th>
<th>Success</th>
<th>2nd Failure</th>
<th>Graft Failure</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP-Thymo</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP-IWG</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Banff 1</td>
<td>N=43</td>
<td>1</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP-Thymo</td>
<td>10</td>
<td>25</td>
<td>6(a)</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP-IWG</td>
<td>8</td>
<td>5</td>
<td>3(b)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>SP+PP+IVG</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Banff 2</td>
<td>N=45</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP-Thymo</td>
<td>11</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>SP-IWG</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>AMR</td>
<td>N=2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP+PP+IVG</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mx</td>
<td>N=6</td>
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<td>0</td>
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<tr>
<td>SP+PP+IVG</td>
<td>2</td>
<td>1</td>
<td>1</td>
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<td>0</td>
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<tr>
<td>SP-Thymo+PP+IVG</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AMR</td>
<td>N=1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Discussion: Pancreas rejection is still a prevalent complication after transplantation. Tailoring anti-rejection treatment according to pancreas pathology, kidney pathology and patient status may result in a more efficient use of immunosuppression. Repeat biopsy can assist differentiate cases or persistent rejection vs resolution of rejection when elevated enzymes or hyperglycemia persists after treatment.

Table 2: Treatment and outcomes according to rejection type and grade for recurrent episodes of rejection cases

<table>
<thead>
<tr>
<th>Rejection Type</th>
<th>No.</th>
<th>Initial Episode</th>
<th>2nd Episode</th>
<th>Success</th>
<th>2nd Failure</th>
<th>Graft Failure</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Banff 1</td>
<td>N=15</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP-Thymo</td>
<td>10</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP-IWG</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>SP+PP+IVG</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Banff 2</td>
<td>N=4</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP-Thymo</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
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<tr>
<td>SP-IWG</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>AMR</td>
<td>N=1</td>
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<td>0</td>
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<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SP+PP+IVG</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mx</td>
<td>N=1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>SP-Thymo+PP+IVG</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chronic rejection</td>
<td>N=1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Discussion: Pancreas rejection is still a prevalent complication after transplantation. Tailoring anti-rejection treatment according to pancreas pathology, kidney pathology and patient status may result in a more efficient use of immunosuppression. Repeat biopsy can assist differentiate cases or persistent rejection vs resolution of rejection when elevated enzymes or hyperglycemia persists after treatment.

Figure: Pancreas Graft Survival

Figure: Kidney Graft Survival

Figure: Patient Survival

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234.7

Prevalence of Type 1 Diabetes Auto-Antibodies in a Large Cohort of Pancreas Allograft Recipients
Delphine Kervella1, Kalyane Bach3, Marine Ollivier2, Lucy Challiboux3, Julien Branchereau1, Georges Karam1, Diego Cantarovich1.
1Institute of Transplantation-Urology-Nephrology, Nantes University Hospital, Nantes, France; 2Institut du Thorax, Endocrinology Unit, Nantes University Hospital, Nantes, France; 3Biochemical Laboratory, Nantes University Hospital, Nantes, France.

Introduction: Type 1 diabetes auto-antibodies seem to be associated to type 1 diabetes recurrence on the pancreas allograft. The aim of this study was to describe the prevalence of type 1 diabetes auto-antibodies and type 1 diabetes recurrence in a cohort of pancreas allograft recipients.

Methods: Between 2017 and 2019, all pancreas allograft recipients (simultaneous pancreas and kidney, pancreas transplant alone or pancreas after kidney) were screened annually for type 1 diabetes auto-antibodies (anti-IA2, anti-ZnT8 and anti-GAD65). Type 1 diabetes recurrence was defined by the following criteria: hyperglycaemia requiring insulin therapy; a severe loss of C-peptide; seroconversion of type 1 diabetes autoantibodies; the presence of insulitis on pancreas transplant biopsy; and the absence of pancreatic rejection.

Results: 244 patients who received a pancreas allograft before 2017 were included. 108 patients (44%) had anti-GAD65 antibodies, 50 (20%) anti-ZnT8 antibodies et 45 (18%) anti-IA2 antibodies. All three antibodies were positive in 11 patients (5%). Type 1 diabetes recurrence occurred in one patient at 6 years posttransplant and was suspected for seven patients in association to rejection of the pancreas allograft. Between 2017 and 2019, 51 patients received a pancreas allograft. Before transplantation, 23 of those (45%) had anti-GAD65 antibodies, 4 (8%) anti-ZnT8 antibodies and 5 (10%) anti-IA2 antibodies. Only one patient had three positive auto-antibodies. With a follow-up of 0 to 2 years, none of these newly transplanted patients had 3 positive auto-antibodies. No case of recurrence occurred in these patients.

Conclusion: We describe a very high prevalence of type 1 diabetes auto-antibodies after pancreas transplantation, but graft loss due to type 1 diabetes recurrence appears to be a rare event.

234.8

Donor-Derived Cell-Free DNA for Rejection Surveillance in Simultaneous Pancreas Kidney Transplantation
Michael Williams1, Mingwei Fei2, Erik Schadde1, Edward Hellingr1, Edie Chan1, Oyedolamu Olaitan1.
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Introduction: Allograft biopsy is the gold standard for diagnosing graft rejection following simultaneous pancreas and kidney (SPK) transplant. Intraperitoneal biopsies are technically challenging, and can be burdensome to patients and the healthcare system. Donor-derived cell-free DNA (dd-cfDNA) is well-studied in kidney transplant recipients, however, it has not been evaluated in the SPK population.

Methods: We hypothesized that dd-cfDNA could be utilized for rejection surveillance following SPK transplant. We prospectively collected dd-cfDNA from 46 SPK patients over a 50-month period at a single institution. Dd-cfDNA was obtained two weeks following transplant, monthly for the first year, then every three months for the next two years, and then every 6 months thereafter. Biopsies were obtained for elevated serum lipase/creatinine, or for elevated dd-cfDNA.

Results: 56 patients were included in the analysis (median age 53, 24% female, median follow-up 2 years). Patient demographics can be seen in Figure 1. 423 total dd-cfDNA values were collected during the study period, with median 8 values per patient. Among all patients, median baseline dd-cfDNA value was 0.18% (IQR 0.15% - 0.22%). Figure 2 shows the trends in dd-cfDNA over time for all patients who were transplanted during the study period. 19 biopsies were performed in total, 5 of which confirmed rejection. There were an additional 5 cases where biopsy could not be performed, but rejection was diagnosed clinically based on clinical factors (sustained dd-cfDNA elevations, rising lipase/creatinine, de-novo or rising donor specific antibodies). These 5 patients were treated for rejection with favorable results, including decreases in dd-cfDNA back to baseline. Among patients who did not have rejection, 97% had dd-cfDNA less than 0.5%. Dd-cfDNA may also help differentiate rejection from other graft injury, with median values in rejection 2.25%, injury 0.36%, quiescence 0.18% (p=0.0006). A pertinent example is a patient with an increase in serum lipase to greater than 20 times the normal value. However, her dd-cfDNA was not elevated (0.35%). Percutaneous pancreas graft biopsy revealed acute pancreatitis without evidence of rejection.

Conclusion: Similar to kidneys, dd-cfDNA shows promise for rejection surveillance in SPK transplant recipients.

Study funded by CareDx, Inc.

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Rejection Injury</th>
<th>Quiescence</th>
<th>P value</th>
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<tbody>
<tr>
<td></td>
<td>N=46</td>
<td>N=13</td>
<td>N=33</td>
<td></td>
</tr>
<tr>
<td>Median Age (IQR)</td>
<td>53 (39-57)</td>
<td>53.7 (38.3-56.7)</td>
<td>53.2 (40.0-57.7)</td>
<td>0.91</td>
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<tr>
<td>Sex (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.70</td>
</tr>
<tr>
<td>Male</td>
<td>35 (76%)</td>
<td>9</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>11 (24%)</td>
<td>4</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Race (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.76</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>7 (15.2%)</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>23 (50%)</td>
<td>8</td>
<td>15</td>
<td></td>
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<td>Hispanic</td>
<td>11 (23.9%)</td>
<td>2</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>3 (6.5%)</td>
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<td>2</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>2 (4.3%)</td>
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<tr>
<td>Transplant Year</td>
<td></td>
<td></td>
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<td>0.12</td>
</tr>
<tr>
<td>2012 - 2015</td>
<td>15</td>
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<td>19</td>
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<tr>
<td>2019 - 2021</td>
<td>12</td>
<td>1</td>
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</table>
A Prospective Study of Donor-Specific Anti-HLA Antibody Monitoring in Pancreas Transplantation

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Introduction: Few studies have evaluated the role of donor-specific antibodies (DSA) in pancreas transplantation (PT). The aim of this study was to analyze the incidence of DSA pre and post-PT and outcomes in a protocol of routine DSA monitoring.

Results: From March/2018 to December/2021, 234 technical successful PT, being 135 SPK and 99 solitary PT (S-PT), of which 86 PAK and 13 PTA, were followed for detection of post-transplant (PT) DSA. All PT received induction therapy with Thymoglobulin, tacrolimus, mycophenolate sodic and steroids. Screening of HLA-antibodies was performed by Luminex at 3, 6 and 12 months PO or when a rejection episode occurred and twice a year thereafter for all S-PT. Any DSA with value >500 MFI was registered. All kidney or pancreas rejection was biopsy-proven and stained for C4d. Pretransplant DSAs were found in 4 SPK and 7 S-PT recipients, all <1500 of MFI. The prevalence of de novo DSA was significantly higher among S-PT, 19(19%), compared to SPK recipients, 12(8.9%), p=0.03, OR=2.43. The average time of DSA appearance was 6.4 months (3-28) and most of them, 25(80.6%), were triggered after a rejection episode. Overall, more rejection episodes were observed in patients with DSA+ than in DSA- (80.6% x 24.1%, p<0.001, OR=13.1). Among SPK patients, DSA+ showed a higher rate of kidney immunological loss (16.7% x 1.6%, p=0.03, OR=12.1), but a similar pancreas immunological loss and kidney, pancreas and patient survival. Among DSA+ S-PT patients, rejection occurred in 16(84.2%), being 12(63.2%) a confirmed or suspected antibody-mediated rejection (AMR). The presence of C4d+ in pancreas graft biopsies was higher among DSA+ S-PT (36.8% x 11.3%, p=0.01, OR=4.6) as was the rate of immunological graft loss (42.1% x 8.7%, p=0.001, OR=7.6), with inferior 1-year (68.4% x 96.2, p=0.001, OR=0.08) and long-term (57.9% x 91.2%, p=0.001, OR=0.13) pancreas graft survival. Mean dosage of tacrolimus (mg/kg/day) among SPK was significantly lower in DSA+ patients in 1st (0.12 x 0.18, p=0.01) and 12th month PO (0.03 x 0.08, p=0.01) and was similar among S-PT (0.14 x 0.13) in all moments. Mean level of tacrolimus (ng/ml) among SPK was similar in all moments (8.41 x 8.22) and was significantly higher in DSA+ among S-PT only in 12th month PO (10.3 x 8.2). Interestingly, long-term pancreas graft survival among S-PT patients was comparable between “weak” DSA+ (MFI<1500) and DSA- (83.3% x 91.3%, respectively) which were significantly higher than DSA+ (MFI>1500) S-PT (46.2%, p<0.001) patients.

Conclusion: Occurrence of post-transplant DSA was higher in S-PT than in SPK recipients, commonly triggered after a rejection episode. De novo DSA was strongly related to higher rate of rejections, AMR, C4d+ pancreatic biopsies, immunological graft failures and inferior pancreas graft survival, particularly if MFI>1500. A protocol of routine DSA monitoring could improve diagnosis and intervention for immunological events after PT.
Using a Unique Repository of Pancreas Transplant Biopsies To Validate the Tissue Common Response Module (tCRM) Score as a Tool to Assess the Severity of Pancreas Transplant Rejection

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Introduction: Analysis of transcriptional data from kidney, heart, liver, and lung transplant rejection led to development of the tissue Common Response Module (tCRM) score based on 11 genes (BASP1, ISG20, PSMB9, RUNX3, TAP1, NKG7, LCK, INPP5D, CXCL9, CD6, CXCL10) which can diagnose the severity of rejection, but have not been validated in pancreas transplant (PT). We aimed to use a unique repository of PT biopsies to evaluate the locked tCRM score and identify additional markers of PT acute rejection (AR).

Materials/Methods: We performed a retrospective study applying gene expression analysis to RNA isolated from formalin-fixed paraffin-embedded tissue from 51 pancreas biopsies, grouped by grade of acute cellular rejection (Grade 1, 2, and 3) versus normal. Gene expression analysis was performed using Nanostring Cancer Immune v1.1 oligonucleotide set of 804 unique genes. Differential gene expression analysis was performed as well as calculation of the tCRM score and pathway analysis to evaluate biological significance.

Results: Significant differences were seen with higher grades of rejection among several transcripts (Fig.1). Of the 22 genes differentially expressed in Grade 3 ACR, 18 were also differentially expressed in Grade 2 ACR. The tCRM score captures the same message with a scaled score that increases across rejection grades (Fig.2). Within the 11 tCRM genes diagnostic of rejection in other solid organ transplants, 9 were significant for PT rejection, with the last two genes (CXCL9 and CXCL10) approaching significance. Within the 11 tCRM genes diagnostic of rejection in other solid organ transplants, 9 were significant for PT rejection, with the last two genes (CXCL9 and CXCL10) approaching significance.

Conclusion: The bulk of AR signal in PT, similar to other solid organs, is attributable to infiltration by activated leukocytes, with background tissue injury specific transcriptional changes. A common hub of immune mediated genes highly significant in rejection (tCRM) and not confounded by tissue source (kidney, heart, liver and lung), were also highly informative for diagnosis and quantification of AR injury in PT. This presents the potential to monitor for rejection using this panel of genes in patients.

Impact of Hypothermic Oxygenated PErfusion (HOPE) During Hypothermic Preservation and Normothermic Reperfusion in a Preclinical Porcine Model of Pancreatic Transplantation

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Purpose: The proportion of pancreatic transplants from standard criteria donors (SCD) is decreasing with a parallel increase in the number of extended criteria donors (ECD) and of marginal donors. Hypothermic Machine Perfusion with (HOPE) or without oxygenation (HMP) are under investigation in kidney and liver transplantation to improve transplants from marginal donors. We propose to evaluate the effect of HMP and HOPE on the in-tissue partial pressure of oxygen of pancreatic transplants during hypothermic preservation and thereafter during reperfusion in normothermic condition.

Methods: We set up a model of marginal donors with a donation after circulatory death in an animal house porcine model (warm ischemia = 30 minutes). After pancreas procurement, pancreatic transplants were preserved during 24 hours in hypothermic condition either in statical cold storage (SCS) (n=4) or on hypothermic perfusion (Waves machine, Institut Georges Lopez) without (n=4) or with oxygenation at 21% (n=4) and 100% (n=4) during 2L/min. Organ preservation solution was IGL-1 and perfusion pressure was 15mmHg. After 24 hours of hypothermic preservation, the pancreatic transplants were reperfused according to a normothermic perfusion model (centrifugal pump system, Sorin Group) without (n=4) or with oxygenation at 21% (n=4) and 100% (n=4) at 2L/min. Organ preservation solution was IGL-1 and perfusion pressure was 15mmHg. After 24 hours of hypothermic preservation, the pancreatic transplants were reperfused according to a normothermic perfusion model (centrifugal pump system, Sorin Group) without (n=4) or with oxygenation at 21% (n=4) and 100% (n=4).

Results: The intra-tissue partial pressure of oxygen of pancreatic transplants during hypothermic preservation and thereafter during reperfusion in normothermic condition.

Conclusion: HMP and HOPE appears to be an effective modality to oxygenate pancreatic transplants during preservation and to conditionate transplants before reperfusion.
Long-term Pancreas Graft Function – What Can We Expect in the Future?

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Background and Study Purpose: Outcome of recent pancreas transplants has improved significantly. Most advances are noted in the first year post-transplant. It is unknown if these improvements in short-term outcome translate to improved long-term outcome. Assessment of long-term outcome depends on length of follow-up time. For transplants performed between 2008 and 2017 the actual follow-up time is not long enough to estimate long-term outcome. A mathematical model is needed to predict and verify long-term graft function.

Methods: Between 1998 and 2017, 21,418 primary deceased donor pancreas transplants (77% SPK, 15% PAK, 8% PTA) in diabetic patients were reported to UNOS/IPTR with follow-up times depending on the year of transplant. Pancreas graft function was defined as insulin-independence and kidney graft function as being dialysis free. Dying with a functioning graft or partial graft function were defined as graft failures. Multivariate Cox regression models for pancreas and kidney graft function adjusted for donor, recipient and transplant factors were developed to functionally describe graft survival during different time periods. The model is based on the first 5 years post-transplant for the years 1998-2012 and the first 3 years for 2013-17 (due to shorter follow-up). Additional models were assessed for transplants which were functioning at 1-year post-transplant. Depending on the time period, half-lives then were estimated. The models were verified for the time periods 1998-02 and 2003-07, for which actual long-term results were available.

Results: Table 1 shows the observed (1998-2007) or estimated (2008-2017) half-lives for the analyzed time period. The differences between observed and estimated half-life for transplants performed between 1998 and 2007 were actually small (2-5 months) so that we can assume that the estimates for the years 2008 to 2017 are reliable estimates. The models show that increased long-term graft function can be expected. Half-life for SPK performed in 2013-17 reached now 17 years for both organs and increases to more than 18 years for transplants that were functioning at 1 year post-transplant. The improved outcomes in PAK showed a doubling in half-life between 1998-02 and 2013-17. This improvement was greatest for grafts that had reached the 1-year time mark as functioning graft. The half-life of PTA also improved over time but did not reach the results of SPK. When a PTA graft is functioning at the 1-year mark, 50% of patients will still have graft function at 8 years post-transplant.

Conclusions: These statistical models not only confirm improvements in long-term pancreas and pancreas/kidney transplantation but also show the expected duration of average graft function in the most recent era. The models underline the importance of function throughout the first year post-transplant and its impact on long-term graft function.

<table>
<thead>
<tr>
<th>Year</th>
<th>SPK Pancreas</th>
<th>SPK Kidney</th>
<th>PAK</th>
<th>PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998-02</td>
<td>137 (176)</td>
<td>156 (170)</td>
<td>77 (194)</td>
<td>77 (118)</td>
</tr>
<tr>
<td>2003-07</td>
<td>157 (179)</td>
<td>160 (178)</td>
<td>87 (121)</td>
<td>72 (132)</td>
</tr>
<tr>
<td>2008-12</td>
<td>172 (195)</td>
<td>178 (187)</td>
<td>101 (123)</td>
<td>71 (88)</td>
</tr>
<tr>
<td>2013-17</td>
<td>201 (223)</td>
<td>208 (217)</td>
<td>144 (200)</td>
<td>80 (103)</td>
</tr>
</tbody>
</table>

Table 1: Observed (1998 – 2007) and estimated half-lives (2008 – 2017). In parenthesis are half-lives for grafts with function at 1 year post-transplant.
Chronic Antibody-Mediated Rejection in Patients Transplanted With Renal Allografts Activates an Inflammatory Amplifying Loop (IL-6+IL-17) When Prolonged IL-6 Secretion Occurs

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¹Nephrology, SGPGIMS, Lucknow, India; ²Clinical Immunology, SGPGIMS, Lucknow, India.

Background: IL-6 is the most important cytokine that plays a central role in the development of chronic inflammation. Recently, non-immune cells like fibroblast have been postulated to mediate chronic allograft rejection via activation of the IL-6 amplifier loop (IL-6+IL-17) via NFκB and STAT3 signaling pathways. We evaluated IL-6 amplifier loop activation by IL-6 and IL-17 in chronic antibody-mediated rejection (CABMR) in renal transplant recipients.

Methodology: Fibroblasts from grafted kidneys from CABMR patients (n=6) were cultured and stimulated with IL-6 (20ng/µl), IL-17 (50ng/µl), IL-6 plus IL-17 for 24 hours. Levels of IL-6, MCP-1, and CCL20 were estimated in culture supernatants by ELISA as markers of IL-6 amplifier loop activation. mRNA expression of IL-6, MCP1, CCL20, and SOCS3 genes were measured in the stimulated fibroblasts. Human Renal fibroblast cells from CABMR patients were lysed with Lysis buffer and subjected to SDS–PAGE and western blotting with anti-STAT3, anti-phospho-STAT3, anti-NFκB p65, and anti-phospho-NFκB p65. Additionally, IL-6, MCP1, and CCL20 levels were measured in Healthy control (n=10), CABMR (n=20), and non-CABMR (n=30) patients.

Results: IL-6 and IL-17 synergistically induced more IL-6, CCL-20 & MCP-1 production from fibroblasts. Gene expression analysis of IL-6, MCP1, and CCL20 was significantly higher with synergistic activation of IL-6 and IL-17 as compared to either IL-6 or IL-17 alone, while SOCS3 gene expression was downregulated. Our results also suggested that IL-6 Amplifier loop activation induces the NFκB and STAT3 signaling pathway activation in the non-immune cells like fibroblast derived from CABMR patients. Additionally, concentrations of IL-6, CCL-20 & MCP-1 in sera were significantly higher in CABMR patients compared to non-rejection patients (p<0.001). There was a significant reduction in IL-6 concentration in culture supernatant with IL-6 and IL-17 inhibitor together and mRNA expression of IL-6 and MCP-1 were significantly reduced.

Conclusion: In humans after kidney transplantation, IL-6 amplifier activation plays an active role in chronic rejection responses. Inhibition of IL-6 with Anti-IL-6 (Tocilizumab) and inhibition of IL-17 with Anti-IL-17 together reduces markers of tissue injury (IL-6, MCP1, CCL20) and rejection of allografts. so, the IL-6 amplifier may be a therapeutic target for chronic transplant rejection.
Prediction of Acute Rejection Post-kidney Transplant: An Artificial Intelligence Approach

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1Renal department, University Hospitals of Coventry and Warwickshire, Coventry, United Kingdom; 2NHSBT, Birmingham, United Kingdom; 3University Hospitals of Mississippi, Mississippi, United States; 4Research Centre for Sport, Exercise and Life Sciences, Coventry University, Coventry, United Kingdom.

Background and Aims: Acute rejection is one of the major risk factors that affects the outcome of kidney transplant. Several immunotherapy protocols have been implemented to prevent acute rejection and improve outcomes. The aim of our study is to use artificial intelligence to build a prediction model for acute rejection episodes in the Tacrolimus era.

Method: All kidney transplant patients registered in UNOS database between 1st of January 2005 and 1st of December 2019 were retrospectively reviewed. Inclusion criteria: deceased donor transplants that were discharged on Tacrolimus/Mycophenolate Mofetil. Exclusion criteria: multiple organ transplants, previous kidney transplants, recipient age<18 years old, living donor transplants, patients not discharged on Tacrolimus/Mycophenolate Mofetil immunotherapy, missing HLA mismatch or ABO incompatible transplant. Patients with complete data were included in the analysis. We performed a CART (classification and regression tree) analysis to build a decision tree for prediction of acute rejection at six months post-transplant. The model evaluation criterion was to maximise recall and minimize false negative prediction. We divided the dataset into training and testing data based on random selection (ratio 70:30). Variables included in the analysis were: recipient characteristics (age, sex, BMI, ethnicity, diabetics, recipient/donor CMV status, time spent on dialysis), donor characteristics (KDPI score) and transplant characteristics (type of induction therapy, steroid therapy at time of discharge, cold ischemia time, delayed graft function, PRA, HLA-A, B, DR, and DQ mismatch). We performed a cost complexity pruning to treat overfitting of the decision tree. We determined the best set of alpha for pruning using optimized cross-validated grid-search for hyperparameter tuning. We created the model where we get highest train and test recall. Feature importance scores were calculated on the weighted Gini indices.

Results: 54,714 patients were included in our study. Figure 1 shows the results of our decision tree. The decision tree recall score was 73.8% in the training data and 66.3% in the test data. Figure 2 shows the feature importance among the decision tree. The most important feature was occurrence of delayed graft function (Relative importance=0.40), followed by age (relative importance=0.14), body mass index (relative importance=0.11), induction with Anti-thymocyte globulin (relative importance=0.8) and 2-HLA-DR mismatch (relative importance=0.7).

Conclusion: Artificial intelligence and decision trees are promising tools to predict the outcomes of kidney transplantation. Delayed graft function, age, type of induction therapy, and HL-DR mismatches are key players in the decision tree to predict acute rejection.
Allograft Vasculopathy in Kidney Transplant Patients: Clinical and Histological Associated Factors

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Introduction: Allograft vasculopathy (AV) defined by arterial intimal fibrosis with mononuclear cell inflammation in fibrosis and formation of neointima is one of the main limiting factors in renal graft survival. The etiopathogenesis is multifactorial, including immune mediated mechanism (chronic active or chronic ABMR or mixed ABMR/TCMR), immune independent factors (e.g., donor age) and the endothelial to mesenchymal transition (ETM). The aim of this study is to evaluate the presence of transplant vasculopathy in kidney transplant biopsies, and the risk factors associated.

Methods: This retrospective study included 400 allograft biopsies for cause in 294 kidney transplant recipient from 2014 to 2018. All biopsies, with and without transplant vasculopathy, donor, recipient and transplant variables were analyzed. We classified the biopsies in Early (< 3 months) and late(>3 months).Clinical variables of the recipient were analyzed: age, anti-HLA sensitization; from the donor: age, alive - deceased; optimal-marginal and transplant process: TIF; mismatch, delayed graft function (DGF); histological features: rejections, microcirculation injury, C4d.

Statistical analysis: Categorical variables are reported as percentages and continuous variables as mean ± standard deviation, median or interquartile range, according to distribution. Chi square test was used to compare categorical variables and T test for continuous variables. Logistic regression models were applied to determine the association of clinical and histological factors with vasculopathy. Odds ratios (OR) with 95% CI were estimated. A p <0.05 was considered significant. The statistical package Medcalc 3.0 was used.

Results: Transplant vasculopathy was found in 51.7 % (207/400) sample biopsies, 40% in the early and 60 % in the late transplant biopsies. Recipient age 46(18-76) years, 57 % men, 11.1 % sensitized and 12.2 % hyper sensitized. 19.3 % had unacceptable antigens and 16.6%(49/294) developed DSA. All patients received induction and triple immunosuppression therapy. Donor age was 46 (10-73) years, 51 % males, 54.4 % deceased donors and 16, 6%(49) met expanded criteria. Mean ischemic time was 16 ± 7 hours, MM 3.5(1.4), DGF 62.3 %. Vasculopathy in early biopsies was associated with ABMR in patients with DSA. In univariate analysis transplant vasculopathy was correlated with male recipient gender (p=0.0354), staining c4d +p=0.029 and chronic glomerulopathy (p=0.0116). Late vasculopathy was associated with c4d +, MVI, late and cellular rejection.

Conclusion: Transplant vasculopathy was correlated with male recipient gender, staining c4d +, and chronic glomerulopathy. Late vasculopathy was associated with c4d +, MVI, late and cellular rejection.

Analyzing the Impact of T-Cell Receptor Diversity in Acute Kidney Transplant Rejection

Tara Sirdal¹, Paul Fields², Juliane Liberto¹, Izabella Damm¹, Maggie Kerwin¹, Jill Hood², Parhoom Towfighi¹, Marina Sirota¹, Harlan Robins², Minnie Sarwal¹.

Purpose: Recent developments in T-cell receptor (TCR) immunosequencing allow for analysis of alloreactive human T-cell populations both before and after engraftment. In this study, we mapped T-cell repertoire from transplant recipients and assessed the role of chronological changes in T-cell clonality, immune repertoire turnover, T-cell Fraction (TCFr), and tissue pathological score to acute rejection (AR) risk stratification and management.

Methods: The study included 339 blood samples, collected before and after transplantation, from 200 kidney transplant recipients; 100 with biopsy confirmed acute rejection (AR), 100 with biopsy confirmed stable (STA) allograft histology. Immunosequencing of the CDR3 regions of human TCRβ locus was performed using the immune SEQ Assay. Sequences were collapsed and filtered in order to identify and quantitate the absolute abundance of each unique TCRβ CDR3 region for further analysis.

Results: More diverse T-cell Repertoire at baseline was associated with AR post-transplant. When compared to STA patients, AR patients had lower (TCFr) before transplantation (p=0.01). After transplantation, patients who developed rejection had greater repertoire turnover (p=0.0024) and increased TCFr. Significant increase in T-cell fraction at late rejection and in ABMR was observed which was significant in late rejection cases >6 mo post-transplantation (p<0.001)(Fig1A). There was an increase in T-cell fraction in ABMR compared to non-ABMR samples (p=0.05)(Fig1B). There was an increased peripheral T-cell fraction among AR subjects compared to STA among AR samples collected at 6 mo post-transplantation (p=0.003)(Fig1C). TCFr also correlated with microcirculation inflammation.

Conclusions: In conclusion, our study demonstrated that T-cell repertoire changes with post-transplant rejection episodes and suggested that the T-cell repertoire changes may provide pre-transplant and post-transplant predictors of rejection risk which in turn can support immunosuppression management decisions at and after transplantation.
Poly (ADP-Ribose) Polymerase (PARP) Expression in Renal Allografts Augments the Development of Epithelial-Tomesenchymal Transition (EMT), Transplant Glomerulopathy, And Interstitial Fibrosis in Pediatric Patients With Antibodymediated Rejection

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Introduction: PARP activation is known to increase inflammation, but its role in developing EMT, interstitial fibrosis (IF), and transplant glomerulopathy (TG) are still unclear. Therefore we investigate the role of PARP in the development of EMT, IF, and TG in recipients with antibody-mediated rejection (AMR).

Method: Expressions of tubular and glomerular PARP, α-SMA, TNF-α, TGF-β, and HLA-DR, were studied in 45 pediatric cases with AMR. Tubular α-SMA expression was noted as tubular EMT. Peritubular capillary (PTC) and interstitial leukocytes were highlighted with PARP, TNF-α, HLA-DR, and CD68. Follow-up biopsies were analyzed for IF and TG development.

Results: PARP expression in tubules, glomeruli, and infiltrated leukocytes was positively correlated with PTC, glomerular, and interstitial leukocyte and macrophage infiltration (p<0.001). Tubular and glomerular PARP expression also correlated with PTC and interstitial leukocyte PARP, TNF-α, TGF-β, and HLA-DR expression (p<0.001). Tubular α-SMA expression (EMT development) positively correlated with tubular, glomerular, PTC, interstitial, PARP, TNF-α, HLA-DR, and CD68 expression (p<0.01). PARP expression increased in tubules, PTCs, interstitium, and glomeruli with the intensity of C4d expression (p<0.01). Response to rejection treatment decreases with increasing tubular, interstitial, PTC, glomerular PARP, TNF-α, HLA-DR, and CD68 expression (p<0.01). IF development time was negatively correlated with the increasing PTC and interstitial leukocyte and macrophage infiltration (p<0.001). The incidence of IF and TG development was found to increase with an increasing degree of renal PARP expression and tubular EMT development (p<0.01). Additionally, the IF development time shortened with increasing PARP, HLA-DR, TNF-α, TGF-β, α-SMA expression in inflammatory and tubular cells (p<0.01).

Conclusion: Increased PARP activation leads to early graft loss by augmenting inflammation and IF by activating inflammatory signaling pathways and tubular cells myofibroblastic differentiation (EMT). Therefore, we suggest that PARP inhibitor drugs combined with immunosuppressive therapy may control inflammation and fibrosis to prevent early graft loss.
Robotic-Assisted Kidney Transplantation (RAKT) in Obese Black Americans (BA) Recipients: Evidence of Healthcare Equity

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Introduction: Morbidly obese patients with ESRD, including Black Americans (BA), may be denied access to life-saving kidney transplant (KT) due perceived higher risk of complications. Robotic-assisted KT (RAKT) is becoming our standard for transplantation in morbidly obese recipients (BMI >40) and is being expanded to the obese population (BMI >30). Our kidney transplant population is >60% BA. With the current particular focus on health equity, we sought to compare the outcomes of RAKT between BA and non-BA recipients at our center.

Methods: A retrospective analysis of all RAKT performed between June 2018 and February 2022 was conducted. Data were compared using student’s t-test and Fisher's exact test (p < 0.05 significant).

Results: Total of 59 RAKT (77% from living donors) were performed with a mean follow up of 19.8 ± 13 months. Majority of RAKT recipients were BA (42/59, 71%) with significantly higher BMI (34.69 ± 6.91 vs. 30.79 ± 6.08, p = 0.04). A significantly higher percentage of BA received kidneys from deceased donors c.f. non-BA (40% vs. 12%, p=0.04). The cold ischemia time was therefore significantly longer in BA group (669.55±639.41 vs. 244.29±257.61 mins, p = 0.005). There was no significant difference between anastomosis and re-warming times despite the higher recipient BMI in BA group. There was no significant difference in patient or graft survival, DGF, peri-operative complications or hospital stay between the two groups.

Conclusions: RAKT yielded excellent outcomes in Black-American recipients despite higher BMI in that group. RAKT could increase access to transplantation, from living as well as from deceased donors, in obese or morbidly recipients who may otherwise be considered ineligible at some centers. The healthcare equity aspects of this approach are particularly affirming.

Table 1 Outcomes after Robotic-assisted Kidney Transplantation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Black American Recipients (n = 42)</th>
<th>Non-Black American Recipients (n = 17)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.24 ± 12.39</td>
<td>46.76 ± 14.55</td>
<td>0.3</td>
</tr>
<tr>
<td>Males</td>
<td>31 (74%)</td>
<td>15 (88%)</td>
<td>0.31</td>
</tr>
<tr>
<td>BMI</td>
<td>34.69 ± 6.91</td>
<td>30.79 ± 6.08</td>
<td>0.04</td>
</tr>
<tr>
<td>Diabetes</td>
<td>18 (43%)</td>
<td>4 (23%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35 (83%)</td>
<td>13 (76%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Donor type</td>
<td></td>
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</tr>
<tr>
<td>Living</td>
<td>25 (60%)</td>
<td>15 (88%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Deceased</td>
<td>17 (40%)</td>
<td>2 (12%)</td>
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</tr>
<tr>
<td>Patient survival 1-year</td>
<td>100%</td>
<td>100%</td>
<td>-</td>
</tr>
<tr>
<td>Graft survival 1-year</td>
<td>100%</td>
<td>100%</td>
<td>-</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>7.61 ± 8.21</td>
<td>6.06 ± 3.07</td>
<td>0.22</td>
</tr>
<tr>
<td>ICU admission</td>
<td>14 (33%)</td>
<td>3 (18%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>18.21 ± 12.83</td>
<td>23.71 ± 12.87</td>
<td>0.07</td>
</tr>
<tr>
<td>S. Creatinine 1-year (mg/dL)</td>
<td>1.77 ± 0.85</td>
<td>1.53 ± 0.28</td>
<td>0.10</td>
</tr>
<tr>
<td>Anastomosis time (mins.)</td>
<td>36.5 ± 10.17</td>
<td>36.29 ± 8.42</td>
<td>0.47</td>
</tr>
<tr>
<td>Re-warming time (mins.)</td>
<td>51.40 ± 14.63</td>
<td>46.61 ± 9.83</td>
<td>0.11</td>
</tr>
<tr>
<td>Cold ischemia time (mins.)</td>
<td>669.55 ± 639.41</td>
<td>244.29 ± 257.61</td>
<td>0.006</td>
</tr>
<tr>
<td>Intra-op bleed</td>
<td>3 (7%)</td>
<td>3 (18%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Conversion to open</td>
<td>4 (10%)</td>
<td>5 (29%)</td>
<td>0.10</td>
</tr>
<tr>
<td>DGF</td>
<td>15 (36%)</td>
<td>3 (18%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Inouveau hernia</td>
<td>0 (0%)</td>
<td>2 (12%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypoxic respiratory failure</td>
<td>2 (5%)</td>
<td>0 (0%)</td>
<td>0.13</td>
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</table>

Robotic-Assisted Kidney Transplants (RAKT) From Living Donors: Single Center Experience

Amit Sharma1, Deki Tsering1, Asmir Khan1, Seung Lee1, Daisuke Imai1, Adrian Cotterell1, Chandra Bhati1, Marlon Levy1.
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Introduction: Obese patients with ESRD may be denied access to life-saving kidney transplant due perceived higher risk of complications. We have adopted Robotic-assisted kidney transplant (RAKT) from living donors as a technique for renal transplantation in this population. We share our experience during our learning curve and compare it with our recently performed RAKTs.

Methods: Consecutive RAKT using kidneys procured with robotic-assisted live donor nephrectomy at our center between June 2016 and August 2021 were retrospectively reviewed and analyzed in two groups: the early (n = 20) versus late (n = 20) experience. Data were compared using student’s t-test and Fisher’s exact test (p < 0.05 significant).

Results: A majority of recipients in both groups (60% vs. 65%) were African Americans (AA). Recipients in our recent experience were significantly older (48.4 ± 12.2 vs. 40.6 ± 14.2, p = 0.03) with higher BMI (34.5 ± 6.04 vs. 29.5 ± 4.4, p = 0.03). There was no difference between the two groups in patient or graft survival or serum creatinine at 1-year post-RAKT. The anastomosis times were not significantly different (35.1 ± 7.7 vs. 32.0 ± 7.3 mins), though the re-warming time (47.7 ± 9.5 vs. 42.0 ± 6.5 mins) was significantly longer in our early experience (p<0.016). There was no significant difference in intra- or post-operative complications. There were no significant differences between the donor age, sex, race, BMI or laterality of the procured kidneys.

Conclusions: Our early and more recent experience demonstrates that RAKT from living donors can be safely performed with excellent outcomes in obese, predominantly African American patients with ESRD. Practice paradigms are evolving to offer RAKT to patients with BMI >40 who may otherwise not be considered eligible for kidney transplantation.

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1Division of transplantation, University of Maryland, Baltimore, MD, United States; 2Division of transplantation, Virginia Commonwealth University, Richmond, VA, United States.

Introduction: Robotic-assisted kidney transplantation (RAKT) is a relatively new surgical technique and remains in its infancy. Few transplant centers are currently performing kidney transplants using this approach. Most centers perform RAKT with hand assistance. We report our experience with full robotic technique.

Objective: To assess the technical feasibility, safety and benefits of the non-hand assisted RAKT.

Methods: We retrospectively analyzed all the robotic-assisted kidney transplants performed from June 2018 to August 2021 at VCU health system. Demographic information of donor, recipient, and technical aspects of the surgery, relevant operative times, post-operative course and complications were recorded and analyzed. These patients were also followed for their kidney function as well as the patient and graft survival.

Results: We performed a total of 45 non-hand assisted purely robotic kidney transplants. Majority of them were from live donors (82%). Demographic profile details in table 1. All kidneys were implanted on the right side and 90% of them were retroperitonealized. There were 12 right kidneys and 33 left kidneys. Three patients required conversion to open because of bleeding from renal vein during attempted retroperitonization and second was converted because of visually pale looking kidney (on conversion kidney was well perfused) and one because of arterial calcification. Most common postoperative complication was hypertension.

Conclusions: Non hand assisted RAKT is a technically feasible procedure and a safe surgical alternative to the standard open approach with excellent outcomes.

RAKT technique

- Complete robotic - non hand assisted approach
- Four robotic Ports and one assistant port
- Gelport placement via umbilicus (7-9 cm incision)
- Camera port via gelport
- Reverse Trendelenburg position
- Goretex suture for vascular anastomosis and PDS for bladder

Demographic profile

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age</td>
<td>40.5 years</td>
</tr>
<tr>
<td>Average operative time</td>
<td>300.0±60.5 minutes</td>
</tr>
<tr>
<td>Median warm ischemia</td>
<td>52 (47 – 62 minutes)</td>
</tr>
<tr>
<td>Median anastomosis time</td>
<td>40 (26 - 49 minutes)</td>
</tr>
<tr>
<td>Average blood loss</td>
<td>208 cc, Median 145 (70-1000 cc)</td>
</tr>
<tr>
<td>Median hospital stay</td>
<td>4 days (3-15 days)</td>
</tr>
<tr>
<td>Mean creatinine at discharge</td>
<td>2.62±1.96</td>
</tr>
<tr>
<td>Mean creatinine at 3 weeks</td>
<td>1.89±1.08</td>
</tr>
<tr>
<td>1 year Graft survival and Patient survival</td>
<td>100 %, 100 %</td>
</tr>
</tbody>
</table>

Surgical and Medical Complications

- Ureteric twist – required revision of anastomosis
- Myocardial infarction – drug eluding stent
- Sub capsular hematoma – laparoscopic drainage
- Wound infection at PD catheter site

Implanting a Robot-Assisted Kidney Transplant Program For Transplant Surgeons With No Robotic Surgery Background

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1Division of Organ Transplantation, Koc University Hospital, Istanbul, Turkey; 2Department of Urology, Koc University Hospital, Istanbul, Turkey.

Purpose: Robot-assisted kidney transplantation (RAKT) was introduced and has been performed commonly by surgeons experienced with robotic surgery. With this single center study we aimed to point out the important steps when we were implanting our RAKT program as transplant surgeons with no robotic surgery background.

Methods: The preparation period was detailed regarding mentors-supervisors, attended courses and, robotic practice prior to the RAKT. We retrospectively analyzed RAKT patients in terms of patient and donor characteristics, indications, console and rewarming times, times for vascular and ureterovesical anastomoses along with the postoperative complications and, patient and graft survivals.

Results: All RAKTs were performed by the same American Society of Transplant Surgeons certified transplant surgeon. First step was the intense simulator training and intense robotic training with vascular anastomosis model followed by the hands-on RAKT training courses at highly experienced institutions. Performing surgeon attended 3 standardized courses at different time points. The same surgeon performed 15 robot-assisted donor nephrectomies prior to the recipient operation. Out of 452 renal transplantation, we performed 24 RAKT between January 2020 and March 2022. The patient request was the indication for all RAKTs. Recipient surgeries were performed with Da Vinci Xi with allografts procured with hand-assisted laparoscopic donor nephrectomy. First 5 cases were carried out under the supervision of expert RAKT surgeons. The median recipient age was 32.5 years (range 16-58 years) with median BMI of 21.7 (range 15.8-33.3). The median console and rewarming times were 226 min (range 155-360 min) and 68 min (range 58-89 min) respectively. The median total vascular anastomosis time was 34 minutes (range 29-50 minutes), while the median ureterovesical anastomosis time was 27 min (range 16-60 min). There was no perioperative complications and 11 patients needed post-transplant blood transfusion. One patient underwent laparotomy for intestinal obstruction. There was no delayed graft function. Overall patient and graft survival rates were 100% with excellent graft function in the median follow up period of 9.6 months (range 0.1-26.3 months).

Conclusions: RAKT requires a very meticulous preparation for transplant surgeons with no robotic surgery background. Well training with standardized hands-on RAKT courses and cooperation between the surgeon and the assistants are crucial to reduce console and rewarming times.
Laparoscopic Nephrectomy for Autosomal Dominant Polycystic Kidney Disease

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1Surgery Kidney Transplant, ITAC by Diaverum, Buenos Aires, Argentina; 2Kidney Transplant, ITAC by Diaverum, Buenos Aires, Argentina.

Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is a monogenic multisystemic disease, characterized by the development of cysts in both kidneys and other extra-renal manifestations. It has a prevalence of 0.1-0.25% and is responsible for 10% of all cases of terminal chronic renal failure (ESRD).

Globally 50% of affected individuals will progress to ESRD. Bilateral nephrectomy adequately resolves symptoms, but studies report a high rate of complications, with 38% morbidity and 3% mortality. Also, concern regarding kidney graft damage or sequelae of the anephric state reduced the percentage of nephrectomies in ADPKD, but Sulikowski et al. reported that more than 40% of patients without pre-transplant nephrectomy needed it later due to multiple complications in native polycystic kidneys. Since the first description of laparoscopic nephrectomy in ADPKD by Elastry et al., they have reported decreased morbidity compared to open nephrectomy. Several authors obtained the same results, both with unilateral and bilateral laparoscopic nephrectomy. In this report, we will carry out a review of the surgical technique, and we will analyze the results obtained by our center with laparoscopic nephrectomy in PKD.

Methods: Retrospectively, we reviewed the medical records of patients with ESRD secondary to ADPKD, who underwent laparoscopic nephrectomy between January 2018 and July 2020. The characteristics evaluated in the patients were: age, body mass index (BMI), surgical indication. Intraoperative and postoperative analysis included duration of surgery, estimated blood loss, hemoglobin drop, blood transfusions, length of hospital stay, pathology, and complications. These were reported using the modified Clavien classification for surgical complications. Surgical technique was summarized in fig 1.

Results: with a study period of 2.5 years, 10 patients (Men: 7, Women: 3) underwent laparoscopic nephrectomy, performing a total of 15 nephrectomies. 4 underwent laparoscopic binephrectomy in 1 stage, 5 unilateral nephrectomy patients, and 1 binephrectomy patient in 2 stages. The surgical indications were: create space for the future transplant in 3 cases, recurrent urosepsis in 6 cases, and recurrent bleeding in 1 case. The preoperative parameters are shown in Table 1. Table 2 shows the perioperative evolution.

Conclusion: Laparoscopic nephrectomy in ADPKD is a safe and effective technique, offering good results and low morbidity to patients. Although open nephrectomy is associated with high postoperative morbidity, such as prolonged hospital stays, postoperative pain, vascular access complications, postoperative ileus, transfusion needs, it continues to be one of the most widespread methods in our environment to treat these patients. Laparoscopic surgery with all the benefits of minimally invasive methods has its place in these patients, achieving very good results.
236.6

Kidney Graft With Vascular Anatomical Variants in a Living Donor Transplant, 20 Years of Experience in a Pediatric Reference Center

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1Transplant - Urology and Nephrology Department, Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; 2Research and Teaching Department, Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; 3Pediatric Surgery Department, Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico.

Introduction: Achieving an ideal kidney graft (KG) for pediatric patients involves a convoluted process. Their chances of survival are reduced by an extended waiting list; leading the need to include KG with vascular anatomical variants to maximize the donor pool and face the existing demand. Such is the case of grafts with multiple renal arteries (MRA) which are a subject of debate that have contradictory results. We present 20 years of experience in KG transplantation with MRA, in a pediatric reference hospital center.

Method: A cross sectional study was conducted. The data of the living donor (LD) consultation from 2001-2021 were analyzed, all KG donors were included in the LD program with MRA and their relationship with the evolution of the donor. We analyzed surgery time, warm ischemia time, bench surgery (BS), donor hospital stay and post-surgical vascular complications in the KG. Descriptive and inferential statistics were obtained using statistical program SPSS 25.0, chi square for proportions and Student’s t-test for means.

Results: In this period 753 patients were evaluated, 175 (23%) MRA grafts were transplanted due to complexity of the contralateral kidney. In 9 (5.1%) of them a right nephrectomy and 166 (94.8%) a left nephrectomy were performed for LD. 151 KG had 2 renal arteries, 23 KG had 3 renal arteries and 1 KG had 4 renal arteries. 131 KG had BS and the rest had vascular anastomosis without BS. Mean surgery time was 87.4 ± 23.9 min (p=0.000), with mean warm ischemia time 217.8 ± 91.2 min (p=0.000). Main surgical findings were 30 (17.1%) cases of venous variants like lumbar vein, retroaortic veins, forked or tortuous veins. 12 cases (6.8%) were arterial variants like accessory arteries, thin, forked or tortuous arteries. There were no complications in 74.2% of nephrectomies. Most common complications were pleural or retroperitoneal opening (14.8%), lumbar vein laceration (1.7%), renal artery injury (1.7%) and degloving of the renal capsule (2.2%). Mean hospital stay was 2.89 ± 2.3 days (p=0.004). The long-term follow up with proteinuria and creatinine depuration levels was similar to single renal artery group.

Conclusion: MRA transplantation is a safe option for donors with similar results to single-artery transplantation in short such in long term. Even though there are significant difference in surgery time, warm ischemia time and hospital stay, the complications associated with the MRA graft are not different from single-vessel graft; considering all nephrectomies were realized only by one surgeon. We conclude that MRA is not a contraindication for renal transplantation in living donors.
236.7

Prophylactic Ureteric Stents in Renal Transplant Recipients; Is Early Removal Associated With Higher Rates of Urological Complications. A Retrospective Analysis of a Single Institution

Michael Funnel1, Jafar Ahmed1.
1Auckland Renal Transplant Group, Auckland City hospital, Auckland, New Zealand.

Background: Renal transplantation is the most effective treatment for end stage renal disease. Urological complications are the most common surgical complication following transplant surgery and can adversely affect patient's outcomes. Prophylactic ureteric stenting has been demonstrated to reduce urological complications significantly. Recently there has been a trend toward shorter duration of ureteric stent placement due to the associated risk of urinary tract infection. The aim of this study was to determine if early ureteric stent removal was associated with higher rates of urological complications.

Patients and Methods: We included all adult patients who underwent renal transplantation at Auckland city hospital over a 12-month period from August 2018 to August 2019. Patient characteristics, surgical and timing of stent removal data was collected. The primary outcome event was hydronephrosis requiring intervention. Secondary outcomes consisted of other urological complications requiring intervention (including perinephric collection and urine leak), total urological complications and urinary tract infections. We performed a multivariate analysis using a logistic regression model to adjust for various patient and surgical variables.

Results: There was a total of 118 patients included in the analysis, 52 had their ureteric stents removed early (post-operative day 4) and 66 had late removal (4 weeks). All patients undergoing renal transplantation had a ureteric stent placed and timing and method of removal was determined by the surgeon at time of surgery. 17.8% of the patients in this study had hydronephrosis that required intervention. We reported a high rate of urological complications, with the significant advantages of less CMV infections. In conclusion, the immunosuppressive combination of low dose Everolimus in combination with reduced-exposure of Tacrolimus (EVR+rTAC) is still limited by lack of evidences from long term follow-up data and by the wound healing issues reported in the early clinical experiences. For these reasons the combination of tacrolimus and mycophenolate mofetil (TAC+MMF) is more frequently adopted as immunosuppressive treatment in renal transplantation. Aim of this study was to analyze clinical safety and efficacy of once a day combination of EVR+rTAC vs standard TAC+MMF in de novo Renal Transplant Recipients (RTR).

Conclusion: De novo use of low dose Everolimus in combination with reduced-exposure of Tacrolimus (EVR+rTAC) is still limited by lack of evidences from long term follow-up data and by the wound healing issues reported in the early clinical experiences. For these reasons the combination of tacrolimus and mycophenolate mofetil (TAC+MMF) is more frequently adopted as immunosuppressive treatment in renal transplantation. Aim of this study was to analyze clinical safety and efficacy of once a day combination of EVR+rTAC vs standard TAC+MMF in de novo Renal Transplant Recipients (RTR).

Methodology: We are reporting our preliminary data of a prospective clinical study in RTR who completed their first 5 years follow-up after renal transplantation. After randomization RTR received once a day low dose EVR (blood levels: 3 - 5ng/ml) plus TAC (blood levels: 3 – 5ng/ml) or standard TAC plus once a day mycophenolate mofetil (MMF+TAC) immunosuppression.

Results: One hundred two renal transplant recipients entered the study and completed the 5 years follow-up. No significant differences were found between the two recipients groups EVR+rTAC (51 pts) and MMF+TAC (51 pts) in the demographic data: age, sex, BMI, time on dialysis, transplant waiting time, native renal disease, pre-transplant diabetes, ischemic heart disease. All patients received as induction low fixed dose of Thymoglobuline (50mg IV x 4 days: pre-op and on day1, 2, 3). The incidence of acute rejection was not significantly different between the two groups (EVR+rTAC: 51 pts) and MMF+TAC (51 pts) in the diagnostic data: age, sex, BMI, time on dialysis, transplant waiting time, native renal disease, pre-transplant diabetes, ischemic heart disease. All patients received as induction low fixed dose of Thymoglobuline (50mg IV x 4 days: pre-op and on day1, 2, 3). The incidence of acute rejection was not significantly different between the two groups (EVR+rTAC: 51 pts) and MMF+TAC (51 pts) in the demographic data: age, sex, BMI, time on dialysis, transplant waiting time, native renal disease, pre-transplant diabetes, ischemic heart disease.

Conclusion: In conclusion, the immunosuppressive combination of low dose Everolimus and low dose Tacrolimus allows the same excellent clinical results of standard Tacrolimus and MMF therapy, without increasing early surgical complications, with the significant advantages of less CMV infections.
Robotic Versus Open Mini-Incision Living Donor Nephrectomy: Single Center Experience

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¹Department of Surgery, Division of Transplant Surgery, Virginia Commonwealth University, Richmond, VA, United States.

Background: A minimally invasive approach is the gold standard for living donor nephrectomy (LDN). While robotic surgery is commonly used for native nephrectomies and urological procedures, robotic LDN is being performed at very few centers worldwide. The robotic platform allows three-dimensional imaging of the surgical site and precise replication of human hand movements scaled down. Robotic surgery is associated with less tissue manipulation and earlier recovery with minimal incision. The aim of this study is to compare the short-term clinical outcomes between robotic-assisted donor nephrectomy (RDN) and open mini-incision donor nephrectomy (ODN) at a single center.

Methods: From 2016 to 2019, 141 consecutive cases involving RDN were analyzed at our single center. Patient outcomes were compared with those from a historical cohort of 191 patients who underwent ODN (7-9-cm incision) from 2010 to 2015. Medical records, including demographics, operation factors, perioperative outcomes, and complications were reviewed retrospectively.

Results: The RDN and ODN groups had a mean age of 42.8 and 41.4 years old, respectively (p = 0.31) as well as a mean BMI of 27.1 and 27.2, respectively (p = 0.76). Left-sided donor nephrectomy was performed in 102 patients (72.3%) via robotic approach and 88 patients (44.7%) via open approach (p = 0.31). Left-sided donor nephrectomy presented <0.001). Operative time was similar between both groups (194.0 for RDN vs. 197.8 min for ODN, respectively; p = 0.40). The RDN group presented shorter in the RDN group than the ODN group (2.34 vs. 3.08 days; p <0.005). The overall rate of complications was low and there was no statistically significant difference in complication rates between the groups. Complications included stump bleeding (3 for RDN vs 1 case for ODN, p = 0.313), urinary retention (1 for RDN vs 3 cases for ODN, p = 0.643), and lymphatic leak (1 for RDN vs. 0 case for ODN, p=0.417).

Conclusions: RDN is a safe and minimally invasive technique with excellent clinical outcomes for living donors. The robotic approach has benefits over the traditional open approach, including shorter length of hospital stay and reduced intraoperative blood loss.

A Systematic Review of Perioperative Outcomes in Robotic Assisted Kidney Transplantation.

Arshad Khan¹, Hoonbae Jeon², Alishta Khan³
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Background: With the advent and accessibility of robotics in surgery in general, RAKT(Robotic-assisted kidney transplantation) is increasingly offered to patients with ESRD. However, the overall advantages over conventional kidney transplants are still debatable. Therefore, this meta-analysis was undertaken to assess the difference in the perioperative outcomes of RAKT versus open Kidney transplantation (OKT).

Methods: Database search was performed following Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) statement to identify studies on the effect of RAKT on surgery duration, kidney failure rate, operative blood loss, length of hospital stay, intraoperative complications, and postoperative complications. The snowball procedure was also used to extract relevant articles from the citations of some included studies. Finally, the Meta-analysis was performed, a random-effects method was applied, and the standard mean difference was used to compute the p-value and I² value.

Results: 10 studies yielding 248 patients in the RAKT group and 750 patients in the OKT group were retrieved for analysis from 327 articles published between 2014 and 2021 that were generated from the database search and another snowballing. The differences in the functional outcomes were not significant across most studies. Of the intraoperative outcomes, pooled results revealed the warm ischemia time (WIT) (SMD = 0.15 [0.33, 0.11], P = 0.11) and operating time (ORT) (SMD = 0.74 [-0.01, 1.48], P = 0.05) had no significant difference in the RAKT and OKT. The pooled rewarming time (RT), and total ischemia time (TIT) were, however, significantly higher in the RAKT compared to OKT, SMD = 1.17 [0.48, 1.85], P = 0.0008 and SMD = 0.87 [0.29, 1.45], P = 0.003 respectively, but there was no difference in pooled CIT SMD = 0.37 [0.13, 0.62], P = 0.27. The blood loss, incision length and anesthesics requirement were significantly lower in the RAKT condition compared to the OKT group at SMD = 0.56 [-0.86, -0.27], P = 0.0002, SMD = -0.38 [-0.72, -1.43], P = 0.004, and SMD = -5.75 [-8.83, -2.67], P = 0.0003 respectively. There was no significant difference for the evaluated postoperative outcome of drain time, and serum creatinine value, SMD = -0.81 [-2.73, 1.08], P = 0.4, and SMD = 0.03 [-0.17, 0.24], P = 0.76 respectively, whereas the length of hospital stay and wound infections was smaller for RAKT SMD = -0.37 [-0.65, 0.08], P = 0.01, and OR 0.20 [0.06-0.62], P=0.006 respectively as shown in figures 1, 2 and 3.

Conclusion: RAKT is a safe and feasible alternative to OKT with the advantages of less postoperative pain, a smaller length of incision, fewer wound infections, and a shorter length of hospital stay with equivalent renal graft function and patient outcomes.

Many thanks to Alishba for retrieving the data.
A Comparison of the Effects of Intravenous vs Oral Hydration on Subclinical Acute Kidney Injury in Laparoscopic Donor Nephrectomy: A Randomised Controlled Trial

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Importance: Laparoscopic and laparoscopic assisted donor nephrectomy is the most common method of donor nephrectomy. Despite improving the outcome for donors by reducing post-operative pain and speeding up recovery, the technique exposes the kidney to additional haemodynamic stresses in terms of extreme position and pneumoperitoneum. Any intervention that could protect the kidney may further improve the residual function of both donated and remaining kidney.

Objective: To determine if preoperative intravenous fluids given overnight, prior to morning kidney donation will result in a measurable improvement in intraoperative haemodynamics and a decrease in subclinical acute kidney injury.

Trial Design: A single centre, prospective single-blinded randomised controlled trial.

Participants: All adult patients aged ≥18 years of age undergoing live donor laparoscopic hand-assisted nephrectomy eligible to participate.

Interventions: Intervention group: The evening prior to surgery, between midnight and 8am, patients in this group will receive three litres of crystalloid solution, IV, in addition to unrestricted oral fluid. Control group: Patients in this group will also be admitted on the evening prior to surgery but will not be given intravenous fluids. They will only receive unrestricted oral fluids.

Main Outcomes: The primary outcome will be a rise in, serum biomarker for acute kidney injury, neutrophil-gelatinase associated lipocalin (N-GAL). Secondary outcomes include donor and recipient renal function, DGF, intraoperative haemodynamics, perioperative complications.

Results: A total of 76 patients (median [IQR] age, 50 [42-57], 44[57%] male) were randomised (36 to preoperative intravenous fluids and 40 to no intravenous fluids) and followed up for 1 year. Serum N-GAL was significantly lower immediately post laparoscopic donation in the intervention group (median [IQR] 103 [90-156], P=.036) but not significantly different at day one post operatively. There was no significant difference between groups in renal function of donors at 6 weeks and 1 year post donation. Intraoperative urine output was significantly higher in the intervention group, but all haemodynamic parameters demonstrated a similar trend between both groups with no significant differences.

Conclusions: Intravenous hydration prior to laparoscopic donor nephrectomy statistically reduces serum N-GAL post operatively but is unlikely to be clinically significant. Therefore, patients undergoing laparoscopic kidney donation would not seem to benefit from admission the day prior to surgery, for intravenous fluid hydration, and could be admitted the day of surgery in keeping with the principles of enhanced recovery protocols.

Selective Ureteric Stenting Is Non-inferior to Routine Stenting for Major Urolological Complications Following Renal Transplant in Low-Risk Patients

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1Central and Northern Renal and Transplantation Service (CNARTS), Royal Adelaide Hospital, Adelaide, Australia; 2Department of Surgery, University of Adelaide, Adelaide, Australia.

Introduction: Major urological complications (MUC) are a significant source of morbidity following a renal transplant occurring in up to 4% of cases. At our institution it has been standard practice to routinely place a J-J ureteric stent across the ureteroneocystostomy at the time of transplant. Meta-analysis has shown reduced incidence of MUC in randomised-controlled trials of stenting with a number needed to treat of 14 to prevent 1 MUC. Despite the potential benefits of routine stenting, evidence suggests there may be no statistical difference between routine vs. selective stenting for low-risk patients in terms of complications such as urinary leak and ureteric obstruction suggesting equipoise for this subgroup. Also, stenting itself is associated with several complications and increased costs such as urinary tract infection (UTI), BK virus and the need to retrieve the stent through flexible cystoscopy. We hypothesised that in select low-risk patients not stenting would be non-inferior to routine stenting in the remainder of our patients.

Study design: After local ethics approval, our prospective observational cohort study was run between June 2017 and June 2021. In this period 380 consecutive renal transplants were performed at our centre. 30 patients were excluded who had dual kidney (including paediatric en bloc) transplant, early graft loss not related to a MUC, duplex ureter in the donor or an intra-peritoneal implantation. Following this, 350 transplants were included for analysis, 240 were stented and 110 were not. Primary outcomes were MUC and UTI and secondary outcome was the incidence of BK viraemia. All transplants used the same technique for ureteroneocystostomy, the Lich-Gregor anti-refluxing anastomosis. The same 3 surgeons performed all transplants used the same technique for ureteroneocystostomy, the Lich-Gregor anti-refluxing anastomosis. The same 3 surgeons performed.

Results: MUC occurred in 6.25% of stented vs. 7.2% of the not stented groups. These included early (<10 days) and late urinary leak, haematuria requiring washout, hydrenephrosis requiring nephrostomy and stent encrustation. Observed rates of urinary tract infection (28.7% vs. 28.3%) and BK viraemia (8.7% vs. 8.1%) were similar between groups.

Conclusions: In our cohort of 350 renal transplants, selectively stenting low-risk patients did not result in a higher rate of MUC. Rates of UTI or BK viraemia were not significantly different. Finally, not needing to remove a stent in our selective group was associated with savings of an estimated $165,000 AUD over 3 years with no statistically significant difference in complications.
ODISSeA: Organ Donation Innovative Strategies For Southeast Asia

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Introduction: ODISSeA is an Erasmus+ project funded by the European Commission. An academic postgraduate programme on organ donation (OD) in 8 Southeast Asian (SeA) universities from Malaysia, Myanmar, Philippines and Thailand was designed and developed. The origin comes from the need for a specialized training that builds adequate knowledge, skills and attitude in OD to increase the well-trained specialists that will efficiently coordinate the process of OD in SeA.

Methods: Training programmes and OD self-assessment (SA) of clinical knowledge (A/n²¹) and of non-clinical competencies (B/n¹₈). SeA universities targeted 3 groups: university personnel, faculty members and potential postgraduate trainees. Train the trainers (TxT) blended programme for SeA trainers healthcare professionals (HCPs). Pre and post course evaluation results were compared. Multilevel blended Postgraduate Programme in Organ Donation (PPOD) targeting HCPs combining academic training (online training and local & international seminars) with bedside projects (On-the-job- projects and awareness events). Pre and post course evaluation results were compared.

Results: Comparing SA results among trainers and trainees in group A 37% vs 54% scored poor to average while 30% vs 20% scored very good to excellent. The overall average score was 9.21 ± 0.39 SD vs 2.49 ± 0.31 SD respectively. In group B 19% vs 35% scored poor to average while 49% vs 25% scored very good to excellent. The overall average score was 3.43 ± 0.67 SD vs 2.83 ± 0.48 SD respectively. HCPs trained in TxT (n41) pre and post testing shows knowledge increase of 15.14% with an overall average score of 6.67 ± 0.96 SD in pre-test vs 7.68 ± 0.66 SD in post-test. HCPs trained in PPOD (n296) pre and post testing shows knowledge increase of 76.45% with an overall average score of 4.6 ± 0.57 SD in pre-test vs 8.12 ± 0.53 SD in post-test.

Conclusion: The innovative approach of ODISSeA as a multilevel educational intervention revealed different results between trainers vs trainees on perception and attitude, clinical knowledge vs non-clinical competencies. Significant knowledge increase was reported upon completion of both, TxT and PPOD. ODISSeA comes to meet the needs identified in deceased organ donation in the SeA region. The project succeeded in establishing recognized academic training in OD in the 8 SeA universities, following the best practices from the most successful European models. Due to covid-19, organ donation decreased in almost all countries worldwide. Malaysia and Thailand were and exception, reporting an increment in the deceased organ donation rates 2020 vs 2019. This increase can be attributed to ODISSeA's implementation and, in the case of Malaysia, to the creation of Organ and Tissue Procurement Units (UPOH) in 16 hospitals, which was translated to a 155% increment in the organ donation family consent rates since UPOH and ODISSeA postgraduate programme began in January 2020.

Acknowledgement to ODISSeA Consortium.
Transplant Procurement Management: 30 Years of International Training Program in Organ and Tissue Donation

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Background: The educational project called Transplant Procurement Management (TPM) was launched in 1991 as a specialised program which main goal is to train health professionals in the field of organ donation for transplantation. Since then, 376 courses have been developed in 44 countries training 15575 health care professionals. The objective is to analyse the impact of the training in the donation rates on those countries where the TPM training has been developed nationally as part of a continuous professional development plan.

Methods: TPM offer is organized by levels (introductory, intermediate, advanced) and training modalities (face-to-face, online, blended), with a result of tailored-made courses according to each country needs. Its core program goes through the clinical process of donation for transplantation and its methodology combines theoretical sessions with hands-on workshops in small groups, simulations, cases discussion and debate. Special attention is given to innovative tools: for donor detection workshop, a videogame has been developed to practice how to detect and evaluate donors in a virtual hospital; to practice communication of bad news and family interview for donation consent, an immersive experience with virtual reality has been designed. The impact of the training has been measured through a retrospective study that includes the organ donation rates published in IRODiAT during the period 2009-2019 in 8 countries and the number of participants registered in our database.

Results: The number of participants trained in these countries from 2009 to 2019 has been as follows: China, 1395; Croatia, 166; Iran, 318; Italy, 2268; Portugal, 301; Slovenia, 263; Thailand, 189; UAE, 283. The donation rates in all countries have increased during the period 2009-2019 in the following: China, 108%; Croatia, 99%; Iran, 394%; Italy, 16%; Portugal, 9%; Slovenia, 24%; Thailand, 217%; UAE, 110%.

Conclusions: An increment of the donation rates has been demonstrated in all countries of the study being higher in those countries with lower initial rates. Therefore, TPM courses have been proven effective in those countries with a national strategy to increase the donation activity that includes education. Education is, among other factors, crucial in the development of donation and transplantation systems at regional or national level. Throughout these 30 years TPM has contributed to the professionalization of health professionals involved in this development and will keep on this endeavour.

An e-Learning Training Program for Communicating Effectively About Vascularized Composite Allotransplantation With Donor Families


Background: Vascularized Composite Allografts (VCA) were added under the definition of organs in the OPTN Final Rule in 2014. However, surrogate decision makers have sole authority to authorize VCA donation. Nonetheless, donor professionals (DPs) have limited experience discussing VCA donation with patient families and many report being unprepared and uncomfortable. Building on over 25 years of evidence-based research, the Communicating Effectively about Donation for Vascularized Composite Allotransplantation (CEaD-VCA), was developed as an e-Learning program to enhance the quality of donor professionals’ communications for VCA donation authorization.

Methods: In partnership with the Gift of Life Institute, the original CEaD program was adapted with the input of OPO professionals. A Learning Management System (LMS) was used to manage participants’ progression through multiple learning modules created as part of the new CEaD-VCA training. CEaD-VCA was evaluated using a nonrandomized per-post design. DPs who obtain family authorization for solid organ donation were recruited from two regional Organ Procurement Organizations and completed an online survey with items assessing their knowledge, preparedness, and confidence for VCA donation discussions. Pre- and post-training responses were compared using paired sample t-tests.

Results: The sample included 42 DPs from 2 OPOs. The majority (71.4%) had at least three years of work experience, but over half (52.4%) had no experience discussing VCA donation with families. Post-training, there were significant increases in mean knowledge scores about VCA (6.4 pre to 7.0 post, p<0.01) and hand (6.2 pre to 8.0 post, p<0.0001) grafts were also observed.

Conclusion: The CEaD-VCA training was effective in increasing DPs’ knowledge, preparation, and confidence when discussing VCA donation. CEaD-VCA is an interactive and easily implementable e-Learning program and holds potential for improving donor professional communication during VCA donation discussions.

Diversity in Organ Donation in Scotland - Improving Awareness in Black and Ethnic Minority Groups

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There is a continued imbalance between the need for organ transplants in Black and Minority Ethnic (BAME) communities in Scotland and the availability of suitable organs with the right blood and tissue type resulting in healthcare inequalities. Currently over 31% of transplant waiting lists in the UK are represented by BAME patients, only 7% of deceased donation are from BAME patients, 75% of opt outs are BAME patients with 70% of BAME families refusing to consent to donation of their deceased relatives. Kidney Research UK along with the Scottish Government and NHS Blood and Transplant have championed the cause of equality of access to information for all faith and cultural groups and their communities to have an understanding of what organ donation means to them. With the change of legislation in Scotland (March 2021) it was even more imperative that people from all backgrounds were made aware that their faith and beliefs can be recorded on the organ donor register. Despite the pandemic, innovative solutions were found on how best to ensure information could be shared not only with local communities but also with faith leaders. The project used the digital platform to host a total of 13 webinars separately with the Muslim, Hindu and Sikh communities and one with Interfaith Scotland. Webinars have been held with local media and the British Medical Association and Café Scientifique and radio and digital magazines such as Asian Voice have aided the dissemination of information. These initiatives include education for health care staff. The project used the digital platform to host a total of 13 webinars separately with the Muslim, Hindu and Sikh communities and one with Interfaith Scotland. Webinars have been held with medical students and the British Medical Association and Café Scientifique. Participation in webinars for nursing staff, staff working in NHSBT and doctors in training have also helped to inform healthcare workers about faith and cultural needs of diverse communities. Engagement with local media such as community radio (Awaz FM and Radio Ramadan) and digital magazines such as Asian Voice have aided the dissemination of information. These initiatives have resulted in positive outcomes with quantity and tone of media coverage and number of events and followers. People at local cultural events, schools and religious places. We have revised Faith leaflets for the Muslim, Hindu and Sikhs faiths with contributions from not just faith leaders but also from the community to ensure accuracy, comprehensibility and accessibility. We are continuing to engage with MSPs from ethnic backgrounds via online meetings to encourage conversations about donation not just amongst their constituents but also in Parliament. While it is difficult to actually quantify the tangible impact on organ donor registrations, continued engagement since 2015 in Scotland with commitment from NHSBT (hosting Scotland’s very first Faith seminar in June 2015) has resulted in an increase in BAME opt ins from 5.8% to 7.8% in 2019-2020. In summary we have harnessed the reach, impact and value of digital and social media platforms to continue this vital piece of work during a pandemic.

International Tissue Banking & Advanced Therapies Training Program: 19 Years of Experience

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Introduction: Since 2003 a Tissue Banking & Advanced Therapies (TB&AT) training program is offered in the framework of the master’s degree in Donation and Transplantation (University of Barcelona). Since 2011, the program had a blended modular (face to face + on-line) structure: donation, transplantation, management, TB&AT, and internship (IS). In 2020, due to COVID-19, it was adapted to be online.

Methods: The aim of the study is to describe the experience of the TB&AT program during the 2003-2022 period and analyze the impact of the pandemics on grades and student’s satisfaction. Until 2020, face to face training included an IS, theoretical sessions, simulations, cases debate and group exercises. Since 2021, theoretical sessions have been included in the virtual classroom and practical simulations have been replaced by live sessions. Immersive training (IT) has been employed to substitute IS. For IS, a virtual reality tour to a simulated tertiary Spanish hospital including a donor tissue center. The TB&AT training is based on the Guide to the Quality and Safety of Tissues and Cells for Human Application of the Council of Europe. Data has been organized in 3 periods, 2003-2010 (1st period), 2011-2020 (2nd period) and 2021-2022 (pandemic period). Participant profiles, grades obtained and the students’ satisfaction has been evaluated.

Results: Since 2003, 1038 participants from 69 countries have attended TB&AT training (411 face to face and 627 on-line). Students grades evolution are: 8,1/10 (1st period, 7,72/10 (2nd period) and 8,24/10 (pandemic period). Participant profiles, grades obtained and the students’ satisfaction has been evaluated.

Conclusion: Comparative results indicate slight difference in the values, demonstrating stability despite the difficulties by the pandemic. The TB&AT training program improves knowledge, technical skills and competence development of the healthcare professionals involved in tissue banking activities. The inclusion of new technologies has been essential to keep offering high quality international educational programs. Further exploring of technologies may also improve efficiency.
Closing the Gap: Addressing Inequities in Access to Kidney Transplantation for Aboriginal Australians From The Kimberley Region

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Introduction: Aboriginal and Torres Strait Islander people are at higher risk of developing chronic kidney disease, particularly those in remote areas, when compared with non-Indigenous Australians. While the number of Indigenous Australians requiring kidney replacement therapy has increased over time, rates of kidney transplantation (KTx) in prevalent patients has remained low at 14% compared with 50% in non-Indigenous Australians.

Methods: The National Indigenous Kidney Transplant Taskforce (NIKTT) was established in 2018 in response to the disproportionately low rates of KTx among Aboriginal and Torres Strait Islander people in Australia. We describe the outcomes of a NIKTT-sponsored initiative developed by the teams at Sir Charles Gardner Hospital, Royal Perth Hospital and Kimberley Aboriginal Medical Service aimed at identifying and addressing modifiable barriers to accessing KTx for Aboriginal Australians with kidney failure in the Kimberley, Western Australia. This remote area which is over 1000 km from the capital city of Perth and spans a vast area of northwest Western Australia caters to the dialysis needs of over 150 Aboriginal Australians.

Results: A multi-pronged approach was used. Culturally appropriate KTx education modules were developed for patients and health professionals in close consultation with Aboriginal liaison officers, Aboriginal health service and the members of the newly established Indigenous Reference Groups (IRG) from the region. These materials were utilised during the small group formal education and informal yarning sessions during the Transplant Outreach Clinics. Work is ongoing to create flip-books and posters. Indigenous Reference Groups were formed across the Kimberley region. Three multi-disciplinary Outreach Clinics were conducted in the region, attended by transplant physicians, surgeons and nurses. This resulted in an increase in the number of Aboriginal patients undergoing assessment from 10 to 71, with 23 being approved for transplant suitability. Several patients were identified to have modifiable barriers to transplant work-up. The number of patients active on the transplant waitlist increased from 4 to 12 within a year of outreach visits. To date, 6 patients from the region have successfully received a transplant. Feedback from patients has been overwhelmingly positive.

Conclusion: Improving access to KTx and transplant outcomes for Aboriginal Australians requires a collaborative, holistic and culturally safe approach to the delivery of care. At the core of addressing the inequity in access to kidney transplantation, is the need to effectively communicate, engage and empower the Aboriginal patients and their communities.

National Indigenous Kidney Transplantation Taskforce Equity & Access Sponsorships, Australia.

The Risk of Venous Thromboembolism Is Enhanced After A Cytomegalovirus Infection in Kidney Transplant Recipient

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Introduction: In immunocompetent patients, past CMV infections have been associated with an increased risk of venous thromboembolism (VTE). In this study, we have investigated in a large prospective cohort of kidney transplanted recipients (KTR) whether the occurrence of a CMV infection which is the most frequent pathogen encountered within the first-year post transplantation could be followed by an increased risk of VTE in addition to the risk of the post-operative period, or repeated hospitalizations.

Methods: We conducted a study on the multicentric DIVAT database which was carried out prospectively and exhaustively on key dates during post-operative follow-up of clinical and biological data for all incident KTR belonging to 8 French transplantation centers (CNIL decision DR-2015-087, N°914184). Multivariable cause-specific time-varying Cox models stratified on centers were used to estimate the relationship between the risk of VTE occurring after well documented first CMV infections (asymptomatic or disease) and which were considered as a time-dependent variable.

Results: 15433 KTR transplanted between 2000 and 2021 were included among whom 1756 presented a CMV infection with a cumulative incidence at 1- and 2 years respectively of 11.6% [95% CI from 11.1% to 12.2%] and 13% [95% CI from 12.4% to 13.5%]. Within the same period of survey VTE occurred in 5.53% (95% CI from 5.17% to 5.92%) and 6.71% (95% CI from 6.31% to 7.14%) at 1- and 2 years respectively of CMV and VTE was observed in 8% KTR. The final multivariable cause-specific time-varying Cox model stratified on centers showed that after a first asymptomatic CMV infection (n=1176) the risk of VTE is 1.61 [95%CI: 1.19; 2.17]. The risk enhanced at 2.00 [95%CI 1.32; 3.02] after a symptomatic infection (n=574) in comparison to similar patients free of CMV infection and independently of recipient age, past history of VTE and post-transplant surgical complications. Finally, the increased risk of VTE occurrence did not change whatever it was a primo or a reactivation of the CMV.

Conclusion: After CMV infections and particularly in case of CMV disease, there is an increased risk of VTE. Since to the high frequency of CMV infection after a kidney transplantation, transplant physicians should be aware of such association for a rapid diagnosis and adapted treatment. The authors would like to thank all patients who participated in this study and the medical and nurse teams who took and take care of them. We also thank the clinical research associates who participated in the data collection and analyses. DIVAT (Données Informatisées et VAlidées en Transplantation) Consortium of the DIVAT Cohort Collaborators (Medical Doctors, Surgeons, HLA Biologists): Lyon Lionel Badet, Antonin Bouchet, Fanny Buron, Sameh Daoud, Vallérie Dubois, François Gaiard, Arnaud Grégoire, Alice Koenig, Charlène Lévi, Louis Manière, Xavier Matillon, Emmanuel Morelon, Maud
Metabolic Characterization of Chronic Antibody-Mediated Rejection (CABMR) Using NMR-Based Serum Metabolomics

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Background: A common complication after renal transplantation is allograft rejection, which often leads to chronic rejection and eventual graft loss. While renal allograft biopsy continues to be considered the gold standard in the diagnosis of chronic rejection, the development of non-invasive methods for the accurate detection of chronic rejection of renal grafts has thus become of important clinical importance.

Methods: NMR-based serum metabolomics was employed for analysis of serum metabolites in 18 renal allograft recipients with chronic rejection and 28 with non-chronic rejection. Samples were analyzed by an 800 MHz NMR spectrometer. The metabolic profiles and differential metabolites of sera were analyzed by multivariate statistical analysis (MSA), including orthogonal partial least squares discriminant analysis (OPLS-DA) methods.

Results: The orthogonal projection to latent structures discriminant analysis (OPLS-DA) model resulted in an R²(Cum) of 0.9 and a Q² (Cum) of 0.5 for CABMR and NCABMR subjects, respectively. Among the differential unregulated metabolites identified in CABMR, citrate, acetyl-carnitine, carnitine, proline, and tyrosine were upregulated from MSA. Citrate had the highest discriminatory potential (AUC 0.8, P=0.0006) followed by carnitine (AUC 0.7, P=0.02, and proline (AUC 0.7, P=0.01). The results demonstrated that CABMR possesses an active Phenylalanine, Tyrosine, and Tryptophan synthesis pathway.

Conclusions: Despite being in its early stages, metabolomics monitoring in kidney transplantation can provide reliable indicators of chronic kidney injuries and allograft rejection. The diagnostic model that evolved in this study may prove valuable as a tool for a definitive diagnosis of CABMR and NCABMR patients after validation in larger sample sizes.
Detection of CMV Mediated Sub-Clinical Rejection by Urine Biomarkers

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Methods: Research on early detection of Cytomegalovirus (CMV) mediated sub-clinical rejection (sAR) is in its nascent stage. This study explores the efficacy of urine-based biomarkers for sAR risk prognostication. Urine samples were serially collected (1 week- 2yrs) across 125 unique renal allograft recipients from UCSF and UCLA. These CMV+ (blood CMV-PCR) patients received valganciclovir therapy until CMV- for 3 consecutive months.

Analysis: We computed a machine-learning based prediction score incorporating urine cell-free DNA (cfDNA), methylated cfDNA, total protein, CXCL10, clusterin and creatinine. Rejection was determined between scores of 32-100; higher score associated with biopsy severity (Yang et al, STEM 2021). In a cross-sectional analysis, Kruskal-Wallis test was performed on the urine-score distribution, to determine sAR during CMV+.

Significance differences were observed in scores >32 between biopsy-confirmed AR vs. stable (p: 0.0034) and CMV vs. stable (p<0.003). Longitudinal analysis yielded 3 primary sAR patterns following CMV infection; (i) persistence of sAR leading to new development of chronic allograft injury; (ii) early sAR (score >32) followed by a further increase in score (>55) with biopsy confirmed cAR; (iii)sAR (>32) followed by recovery of injury with CMV resolution and a decline in score <32).

Conclusions: We provide a urine-based method for detecting sAR at the time of CMV infection, and its potential clinical utility for titrating use of antiviral therapy and recipient immunosuppression load.

Cytomegalovirus-Induced Thrombotic Microangiopathy After Renal Transplant: Case Report and Review of the Literature

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Introduction: CMV infection as a triggering factor for de novo post-transplantation TMA has long been suggested. We herein report a case of CMV and BKPyV co-infection in a kidney transplant recipient and CMV-induced TMA manifested by severe AKI and thromboticmicroangiopathy.

Case report: A 48-year-old man with end stage kidney disease secondary to diabetes mellitus underwent a 4 HLA-mismatched, deceased donor renal transplant from a 40-year-old donor who died of a cerebrovascular accident. Cold ischemia time and warm ischemia time were 51 and 18 minutes respectively. CMV IgG was positive in donor and negative in recipient. Intraoperative methylprednisolone and antithymocyte globulin were used for induction for anticipated delayed graft function. He was discharged on postoperative day 6 with a serum creatinine (SCr) of 8.1 mg/dL. His allograft function continued to improve, achieving a SCr of 1.67 mg/dL at 1-month post-transplantation. His SCr had since fluctuated between 1.4-1.7 mg/dL. At 4-month post-transplantation, he was found to have low grade BK DNAemia (900 copies/mL) managed with mycophenolate dose reduction alone. He did well until 14-month post-transplantation when he presented with non-oliguric AKI with a SCr of 240.4 mg/dL requiring dialysis initiation. Peripheral smear demonstrated thrombocytopenia but no schistocytes. A renal allograft biopsy (figure 3) was performed which revealed BM nephropathy, TMA, and no evidence of rejection. Labs revealed CMV DNAemia of >140,000 copies/ml and BK DNAemia of 17,000 copies/ml. Donor was tested positive for CMV, M RNA polymerase chain reaction (PCR), hepatitis C RNA PCR, antiadcollin anti-body, stool shiga toxin PCR, and stool and blood cultures were all negative. Intravenous ganciclovir was initiated with improvement in CMV DNAemia and concomitant improvement in renal function. He was transitioned to oral valganciclovir after 10 days of intravenous therapy with complete resolution of CMV DNAemia and steady improvement in renal function. His SCr continued improve and nadled at 1.7 mg/dL. At 2-year follow-up, his SCr was 1.74 mg/dL.

Discussion: Initiation of IV ganciclovir and reduction in CMV DNAemivith decrease in SCr and a transition of the patient off hemodialysis suggested that CMV is the causative factor for TMA. CMV-induced renal injury can manifest as various histopathological patterns, commonly as a CMV glomerulopathy with viral inclusions usually seen in the glomerular endothelial cells, acute tubulointerstitial nephritis and rarely as TMA. Improvement in renal function despite continuation of tacrolimus in current patient suggested that calcineurin-inhibitor-induced TMA was unlikely. Although the precise mechanism whereby CMV viremia may cause TMA is currently not fully understood, it is speculated that infection can initiate endothelial cell damage and inflammation which triggers the thrombotic cascade leading to TMA.
Parvovirus B19 Disease Post-renal Transplant Presenting as Refractory Anemia - Case Series of 20 Patients

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Introduction: Transplant patients are susceptible to a wide range of infections, one of which includes Parvovirus B19 (PVB19). In a post-renal transplant patient, due to failure to mount a neutralising antibody response to the virus, PVB19 causes significant morbidity & also graft dysfunction. It is usually present in the first year of the post transplant period, associated with anemia and non specific signs and symptoms.

Methods: We retrospectively reviewed all transplant recipients from the period 2013 to 2020. 20 recipients were found to be positive for Parvovirus B19, when tested for evaluation of anemia. We looked at the epidemiology, clinical spectrum and outcome of patients with post-transplant PVB19 infection. Parvovirus B19 polymerase chain reaction (PCR) was done for all patients for the diagnosis. Bone marrow examination (BME) was also performed on 8 patients for the diagnosis. Bone marrow examination (BME) was also performed on 8 patients.

Results: The prevalence of Parvovirus infection was 2.16% (20/924). The median time to onset of PVB19 disease was 39 days post-transplantation. Clinical presentations include fever, generalized weakness; dyspnea and myalgia in 50%, 75%, 25% and 40% respectively. Anemia, leucopenia, and thrombocytopenia were present in 100%, 20%, and 10% of patients, respectively.

50% of patients with Parvovirus disease had graft dysfunction evidenced by a 30% elevation in the serum creatinine from baseline. 5 patients developed PVB19 after treatment for acute rejection and 4 patients developed acute rejection after reduction in the immunosuppression for treatment of PVB19. Almost all patients (95%) had a positive PVB19 PCR and the remaining one patient had Typical Giant cell on Bone marrow aspiration. Hypocellular marrow was seen in 87.5% of patients who underwent BME. Reduction in Immunosuppressant therapy was the most commonly used modality of treatment. IVIG, Packed cell transfusion and Erythropoietin therapy were also used. Two out of 20 patients had their graft lost.

Conclusion: ParvovirusB19 is a rare but clinically significant cause of as refractory anemia during the early post-transplantation. The use of PCR for diagnosis and reduction in immunosuppressants particular antiproliferative agents is the mainstay of treatment.
The Age of the Recipient and the Ratio of CD4/CD8 in Renal Allografts Influences the Prognosis and the Presenting Time of the Polyoma Virus-Associated Nephropathy (PVAN)

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Introduction: Uremia and hemodialysis (HD) are the primary pro-inflammatory conditions that can cause pre-mature immunological aging, virtually known to be unchanged after the transplantation. Drop in the CD4/CD8 ratio is the most critical consequence of immunological aging. Therefore, we aimed to understand the influence of the recipient’s age and the ratio of CD4/CD8 on the prognosis and the presenting time of the PVAN in renal allografts.

Method: All 71 patients separated into three age groups [Group P ≤20 years (n:22), Group A: 20-50 years (n:30), Group B >50 years (n:19)]. Interstitial CD68, CD3, CD4, and CD8 positive cells graded. Patients were also separated into two groups in regards to the time of PVAN development [Group 1 (n:48) (≤12 months) and Group 2 (n: 23) (>12 months)]. Follow-up biopsies were evaluated for interstitial fibrosis (IF).

Results: The mean interval between the PVAN and transplant was 17±22 months. The presenting time of PVAN was found early in Group P (8,9±6,8 months) and B patients (8,6±8,2 months) than Group A (28,8±19,9 months) (p=0,001). Most of the patients in Group 1 were from Group P (n:22/22, 86,4%) and Group B (16/19, 84,2%) while only a few of them were from Group A (n:13/30, 43,3%) (p=0.001). The mean HD time was higher in Group P and B than in Group A (p=0,01). Group P (0,84±0,6) and Group B (0,77±0,6) patients showed lowest mean CD4/CD8 ratio compared to Group A (1,47± 0,9) (p<0.01). Also, the mean CD4/CD8 ratio was lowest in Group 1 recipients than group 2 (p<0.001). CD4/CD8 ratio negatively correlated with mean HD time, Pvl, viremia, and viruria (p<0.01) in all age groups. Total 43 patients developed IF, and 31 (43,7%) cases lost their graft. The mean CD4/CD8 ratio correlated positively with IF and graft loss (p<0.05).

Conclusion: Pediatric and old age groups have a lower CD4/CD8 ratio than adult patients aged 20 to 50 years. Pediatric and old age groups tend to show early onset of PVAN with an increased risk of IF development and graft loss associated with the low CD4/CD8 ratio.
240.7

Macrophages and Different Subtypes Infiltrated in Kidney Allografts With Antibody-Mediated Rejection

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Objective: To clarify the degree and location of total macrophages and subtypes infiltrated in the kidney allografts with antibody-mediated rejection (AMR) and its possible mechanisms.

Methods: There were three groups of renal biopsy, normal kidneys as the control group, renal allografts with stable renal function after kidney transplantation as the stable group and renal allografts with AMR diagnosed by biopsy after kidney transplantation as the AMR group. After fixed with 4% paraformaldehyde, embedded in paraffin and sectionalized, these tissues were stained using immunohistochemistry (IHC) to observe the positive degree and location of markers CD31, CD68, CD86 and CD206.

Results: Pathological changes in the three groups matched the previous description according to Hematoxylin-Eosin (HE) and Periodic Acid-Schiff stain (PAS) staining. Compared with the control group and stable group, the number of total macrophages (CD68+) infiltrated in the AMR group was significantly increased, and the infiltrated macrophages were mainly distributed around the microvessels (glomerulus and interstitial capillaries)(CD31+). Further classification of the infiltrated total macrophages in the AMR group showed that these macrophages were mainly pro-inflammatory M1 macrophages (CD68+CD86+), while the infiltration of tissue repair associated and anti-inflammatory M2 macrophages (CD68+CD206+) was not significant.

Conclusion: When AMR occurred in renal allografts, macrophages were mainly infiltrated around microvessels and they were largely pro-inflammatory M1 subtype. We hypothesized that chemotactic macrophages from endothelial cells of microvessels infiltrated into the transplanted kidney and were involved in the pathogenesis of AMR.

240.8

Outcomes of Kidney Transplantation in Recipients Exposed to the Risk of Chagas Disease Reactivation

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1Renal Transplant, Hospital de Clínicas, Porto Alegre, Brazil; 2Postgraduate degree, UFRGS, Porto Alegre, Brazil.

Introduction: Chagas disease (CD) affects approximately eight million people worldwide, implying that, in the endemic regions, a large number of donors/recipients are exposed to contaminated organs. Symptoms range varies from asymptomatic to severe cardiac and digestive complications. Therefore screening is vital since immunosuppression predisposes to disease activation.

Method: A retrospective uncontrolled cohort study with renal transplant recipients (RTR), performed between 2012 and 2020, with recipients with positive serology for Chagas disease (R+), donors with positive serology (D+), or both positive (D+ and R+). Patients were identified by reviewing medical records or dispensing Benznidazole used in the postoperative period. Patients were monitored for CD recurrence by parasitemia, serology, and PCR.

Results: Fifty-three deceased donor KTR were included, 36 men (67.9%), 51 caucasoid (96.2%), with a mean age of 53.9±12.4 years. The cause of renal failure was from undetermined etiology in 17 patients (32%), diabetic nephropathy in 10 patients (18.8%), and hypertension in 9 patients (16.9%). In all transplants, there was a positive serology for CD. There were 40 positive donors (75%), nine positive recipients (16%), and in four cases, both the donor and the recipient were seropositive. All patients received post-transplant prophylaxis with benznidazole at a 100–500 mg/day dose for 4-90 days (median for 22 days). One patient presented urticaria and angioedema as an adverse event determining early benznidazole discontinuation. The most commonly used initial immunosuppressive regimen was thymoglobulin (ATG), sodium mycophenolate (MFS), and methylprednisolone in 25 patients (47.1%), and 40 patients (75.4%) received a regimen containing ATG. The maintenance immunosuppression consisted of MFS, tacrolimus, and prednisone in 51 patients (98%). The incidence of acute rejection in the first year after transplantation was 11% (six cases). No cases of Chagas disease reactivation occurred. Patient and graft survival rates were 75% and 81%, respectively, five years after grafting.

Conclusions: Chagas disease-positive serology, either in the donor, in the recipient, or both, in KTR receiving benznidazole prophylaxis, allowed more patients to be transplanted. The primary transplant outcomes were similar to those observed in KTR not exposed to Chagas disease.
Primary-Infected Renal Allograft: Variants of the Clinical Picture and Outcomes

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¹Kidney & Pancreas Transplantation, SRI for Emergency Care N.V.Sklifosovsky, Moscow, Russian Federation; ²Department of transplantation and artificial organs, Moscow State University of Medicine and Dentistry, Moscow, Russian Federation; ³Methodic and organization department for organ transplantation, Scientific-research Institute of Health Organization and Medical Management, Moscow, Russian Federation.

Background and Aims: In some cases the KG’s storage solution turns out to be contaminated. This asymptomatic donor’s bacteremia can threaten the recipient’s health and life, because of leading to various infectious complications. Moreover, primary graft infection is detected several days after surgery. The aim: to explore options for the clinical course and outcomes after primary-infected kidney transplantation.

Methods: we analyzed 1633 KTx. 72 cases of primary-infected renal allograft (PIRAG) transplantation were identified. All PIRAG’s recipients were initially prescribed immunosuppressive therapy (IST) and antibacterial prophylaxis with 3rd gen of cephalosporins. The bacteriological research results were obtained on the 3-7 day after KTx. Having a positive result, the therapy was immediately adjusted according to the individual sensitivity of infection to antibiotics.

Results: In 47.2% cases, the Gram+ or - flora had been detected. Mixed infection - in 4.2% cases. Yeast fungi - in 1.4% cases. There were no any infectious complications in 72.2% of PIRAG cases. In 16.7% the development of local and/or generalized purulent-septic complications with the development of sepsis had been noted immediately (on 2-5 days after KTx). In such cases, emergency nephrotransplantectomy, revision, sanitation and drainage of infected areas were performed. Antibiotic therapy was prescribed, IST was canceled, and intravenous administration of human immunoglobulin was used. In cases of arrosive bleeding from the vessel’s anastomoses we performed the recipient’s external iliac artery and vein resection with simultaneous cross-iliac-femoral shunting. In 11.1% delayed complications with satisfactory graft’s function had been manifested.

Conclusion: PIRAG is an undoubted factor of septic complication’s development in kidney recipients. While PIRAG detected, the immediate antibacterial therapy maximization is necessary, with its correction according to microflora’s sensitivity to antibiotics.

Effect of Mycophenolic Acid and Tacrolimus on the Incidence of Infectious Complications After Kidney Transplantation

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Introduction: Infectious complications remain a common cause of mortality after kidney transplantation (KTx). Goal of effective immunosuppressive treatment must be balanced between the decreasing incidence of acute kidney rejection (AKR) and at the same time avoiding the incidence of infections.

Materials and methods: The aim of our analysis was to identify the risk of fixed daily dose (DD) of mycophenolic acid (MPA) and levels of tacrolimus (TAC) in the development of a single, recurrent infection and AKR after KTx.

Results: Our analysis consisted of 100 patients after KTx (66 males, 34 females). MPA daily dose > 1080 mg was a risk factor (RF) for recurrent infection in general (OR 1.2964;P=0.0277), for recurrent bacterial infection from 1st-6th month (OR 1.2674;P=0.0151), recurrent bacterial infection (OR 1.2574;P=0.0436), single viral infection (OR 1.2640;P=0.0398) from 6th-12th month after KTx. Daily dose of MPA > 1080 mg and levels of TAC above recommended levels were not independent RF for the incidence of the infection.

Conclusion: Daily dose of MPA > 1080 mg as a RF for recurrent infection starting in the 1st month after KTx with significant association between the incidence of infections and MPA daily dose and TAC levels, without increased risk of AKR. In the centers with fixed dosing of immunosuppression, this can lead to lowering the risk of infections by decreasing daily dose of MPA 1 month after KTx without increasing risk of infections.
Role of Norovirus Infection in Kidney Transplant Recipients Presenting With Persistent or Chronic Diarrhoea

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Background and Objective: Persistent and chronic diarrhoea is a significant problem in the kidney transplant recipients. It is associated with significant weight loss, morbidity and graft dysfunction. Norovirus infection has emerged as important etiology of chronic diarrhoea in kidney transplant recipients. In absence of any specific therapy, mainstay of treatment is supportive care and immunosuppression reduction. There is paucity of data regarding role of Norovirus infection in Indian patients. Aim of our study was to evaluate role of Norovirus in kidney transplant recipients presenting with persistent or chronic diarrhoea.

Method: 39 kidney transplant recipients presenting with persistent or chronic diarrhoea were enrolled. Stool for Norovirus RTPCR was performed using TaqMan real-time reverse transcription-PCR assay (Fast-track diagnostic: FTD 45–64 Kit). Patients were followed up for 12 months.

Results: 29 out of 39 patients were positive for Norovirus RTPCR in stool. Median duration of presentation from transplant was 63.5 months (range 12.4 to 143.4 months). Median duration of diarrhoeal symptoms prior to presentation was 60 days (range 14 to 365 days). All patients had significant weight loss on presentation. Mean weight loss was 6.3 ± 3.3 kg. 7 (24%) had persistent weight loss and 3 (10.3%) had steady weight at 12 months of follow up. 18 (69%) patients had AKI at enrolment. 14 out of 27 (48%) patients completing 12 months follow up had worsening of renal function at 12 months, 4 (15%) were on maintenance haemodialysis.

Immunosuppression modification was done in 26 (89.6) of patients in Norovirus positive group. Antiproliferative medication reduction or withdrawal was the initial approach. 6 patients were switched from tacrolimus to cyclosporine. 7 (25%) patients had persistence of intermittent diarrhoea at 12 months. Norovirus was detected in 5 patients at 3 months follow up. At 6 months, 4 out of 8 patients had Norovirus detection in stool. At 9 months, 3 out of 4 patients had positive Norovirus RTPCR. Norovirus was detected in 9 of 11 samples evaluated at 12 months of follow up.

Interpretation and Conclusion: Norovirus is the most common cause of persistent and chronic diarrhoea in renal transplant recipients. It is seen late after transplant and is associated with significant weight loss and graft dysfunction. Immunosuppression reduction is associated with improvement in diarrhoea and weight gain in majority of patients. However, renal function may not improve. Viral shedding may continue despite improvements in symptoms.

<table>
<thead>
<tr>
<th>Overall Renal Outcome</th>
<th>Noro Positive (n = 29)</th>
<th>Noro Negative (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI at enrolment Mean Creatinine (mg/dl)</td>
<td>18 (62%) (2.42 ± 0.69)</td>
<td>7 (70%) (2.35 ± 1.11)</td>
</tr>
<tr>
<td>No AKI at enrolment Mean Creatinine (mg/dl)</td>
<td>11 (38%) (1.67 ± 0.43)</td>
<td>3 (30%) (1.4 ± 0.35)</td>
</tr>
<tr>
<td>Worsening of renal function at 12 months</td>
<td>14 (48%) 4 on MHD</td>
<td>2 (29%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Noro RTPCR</th>
<th>Positive n = 29</th>
<th>Negative n = 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight before onset of diarrhoea (mean ± SD; kg)</td>
<td>63.1 ± 11.3</td>
<td>62.92 ± 9.4</td>
</tr>
<tr>
<td>Weight at enrolment (mean ± SD; kg)</td>
<td>56.7 ± 11.1</td>
<td>56.98 ± 7.86</td>
</tr>
<tr>
<td>Weight loss (mean ± SD; kg)</td>
<td>6.3 ± 3.3</td>
<td>6.7 ± 4.7</td>
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<table>
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<tr>
<th>Completion of 12 months follow up (total)</th>
<th>n = 27</th>
<th>n = 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with persistent weight loss</td>
<td>7 (24%)</td>
<td>3 (43%)</td>
</tr>
<tr>
<td>Patients with weight gain</td>
<td>17 (58.6%)</td>
<td>4 (57%)</td>
</tr>
<tr>
<td>Patients with steady weight</td>
<td>3 (10.3%)</td>
<td>-</td>
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Maturation and Evaluation of 3D Printed Bionic Pancreas With a Dedicated Bioreactor

Andrzej Berman¹, Marta Klak¹, Tomasz Dobrzanski¹, Mateusz Szczygieleśki¹, Sylwester Domanski¹, Marta Kołodziejška¹, Iwo Koronowski¹, Michał Wszola¹.
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The technology of 3D printing of bionic organs gives an opportunity to solve the problems of classical transplantology, such as the shortage of organs, complications of immunosuppression or rejection. After printing, the bionic pancreas requires an optimal environment conditioning the process of its maturation, which consists in the colonization of the produced vessels with endothelial cells and the tubularization of the endothelium within the microcirculation. After the maturation process is completed, it is necessary to evaluate the resulting organ in terms of its functionality and safety.

In order to minimize the risk of contamination while ensuring the necessary functionalities, a bioreactor was created that allows the maturation of the bionic pancreas, and after the end of the process, functional assessment using the semi-automatic Glucose-Stimulated Insulin Secretion (GSIS) test and the assessment of vascular tightness using the pressure test. 10 procedures of maturation and bionic pancreas evaluation were performed using a bioreactor. 5 pancreas contained human beta cells (45000 000 cells) and 5 pancreas contained porcian isolated pancreatic islets (75,000 IEq). The mean pancreatic maturation time was 23 hours (2-72 hours). The effectiveness of adhesion of endothelial cells to the vascular wall and tubularization of endothelial cells was assessed by immunohistochemistry. The GSIS test was performed by automatically replacing the medium with glucose at various concentrations. The integrity of the vascular system was assessed by maintaining a pressure of 190 mmHg for 5 minutes.

The adhesion of endothelial cells to the bioink was observed after 1 hour. Tubularization of the endothelium was observed after 48 hours. Insulin secretion upon stimulation with glucose was observed without delay to the control (beta cells or islets) and the insulin concentration during the observation showed a constant ratio compared to the control, but without a clear peak at high glucose concentration. In 8 out of 10 pancreas, no vascular leakage was observed during the pressure test. No material contamination was observed during pancreatic perfusion. The use of a dedicated bioreactor enables safety during the bionic maturation process of the organ, while allowing for an effective assessment of the organ’s functionality and the tightness of the vascular system.
241.2 A Worldwide Survey of Activities and Practices in Clinical Islet of Langerhans Transplantation


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Background: The lack of a comprehensive international islet transplantation registry has prevented full visibility of worldwide islet transplantation activity.

Methods: A global online survey was administered to 69 islet transplantation programs, covering 84 centers and 5 networks, using Microsoft Forms. The survey addressed questions on program organization and activity in the 2000-2020 period, including impact on activity of national health care coverage policies. Impact of the COVID pandemic was also addressed. Activity data from non-responding or not contacted centers were obtained from the CITR or other sources.

Results: The survey response rate was 88%. We obtained full data from 55 institutions or networks worldwide and basic activity data from 6 centers. Additional data were obtained from alternative sources. A total of 94 institutions and 5 networks was finally identified as having performed islet allotransplantation. 1321 islet allotransplants (2,565 in Europe, 1,475 in North America, 135 in Asia, 119 in Oceania, 28 in South America) were reported in 2,149 patients in the survey period. From 15 centers active at the start of the study period, the number of simultaneously active islet centers peaked at 54, to progressively decrease to 26 having performed islet allotransplants in 2020. Notably, only 16 centers/networks have done >100 islet allotransplants in the survey period. Types of transplants performed differed notably between North America and the rest of the world, in particular with respect to the near-absence of simultaneous islet-kidney transplantation and the significant number of centers performing only islet autotransplants. Absence of health care coverage has significantly hampered transplant activity in the past years and the COVID-19 pandemic in 2020.

Conclusions: This comprehensive survey was able to quantify islet transplant allotransplantation in the last 2 decades and identify differences in activity and practices in different world regions.

241.3 Generation of Prevascularized Endocrine Constructs to Treat Type 1 Diabetes

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Introduction: The goal of our study was to generate a functional, prevascularized endocrine constructs utilizing amnion membrane derived hydrogel, islets and blood outgrowth endothelial cells (BOECs) to be transplanted in diabetic hosts.

Methods: Human amniotic membranes were dissected from placentas decellularized, lyophilized, and solubilized to obtain hydrogels. DNA quantification and scanning electron microscopy showed complete removal of cellular components and preserved extracellular matrix. Characterization studies demonstrated widespread distribution of all essential structural proteins, including collagen, GAGs and laminin. The islets and BOECs were admixed in amnion derived hydrogels and cultured in specially designed media to enhance endothelial cell assembly into tubular, vascular-like structures. Constructs were kept under culture for 3 days. Glucose stimulated insulin secretion (GSIS) tests showed an adequate insulin secretion in response to high glucose stimulation, confirming the functional activity of the prevascularized endocrine constructs.

Results: To test in vivo biocompatibility and function, the vascularized constructs generated from 500 IEQ rat islets and 2×10⁵ human derived BOECs were implanted under the skin of the diabetic NSG mice. Transplantation of the constructs led to rapid and long-term (90 days) normalization of blood glucose levels. Removal of the grafts led to recurrence of hyperglycemia within 24 hours, indicating that the transplanted constructs was responsible for normalized glucose levels. Histological analysis of the explanted grafts revealed healthy islet morphology and perfect revascularization. Grafts stained positive for insulin and human specific CD31 indicating presence of human endothelial cells in newly formed intra-islet micro vessels.

Conclusion: Our findings show that amnion derived hydrogel seeded with endocrine pancreatic tissue and endothelial cells could be used for functional, prevascularized endocrine construct bioengineering.

This work is supported by grants from the European Commission (Horizon 2020 Framework Program: VANGUARD grant 874700), the European Foundation for the Study of Diabetes (EFSD), the Juvenile Diabetes Research Foundation (JDRF; grant 3-SRA-2020-926-S-B) and the Shota Rustaveli National Science Foundation (grant FR-19-19760).
Chagas Disease (CD) After Hematopoietic Stem Cells Transplantation (HSCT). Incidence, Diagnosis and Management

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1Bone Marrow Transplant, Fundacion Favoloro Hospital Universitario, Caba, Argentina.

Introduction: Although CD could be transmitted by blood products and organs transplantation, HSCT might be performed safely in patients (pts) affected or with donors (D) infected with trypanosoma cruzi, the etiological parasite. CD reactivation could be triggered by immunosuppression. Early diagnosis and an adequate treatment are essential to overcome this situation.

Patients and methods: From October 2001 to February 2022 a total of 1604 pts and D, aged 9 m. to 77 years-old, were pre-transplant or hematopoietic cells donation screened for CD with 2 of the available serological tests: immune hemagglutination, immunofluorescence assay, or ELISA. A double positive result was considered as a marker of CD. Pts and D detected positive were further tested by one parasitological method: Strout (from 2001 to 2010) or PCR specific test (from 2010 to 2022). Only Pts and D with a positive parasitological test were treated with benznidazole 5mg/kg/D during at least 4 weeks or until reach a negative status. HSCT or cells donation were postponed unto tested negative. In the post-transplant period, in pts with positive serology, a pre-emptive treatment strategy with benznidazole was implemented. PCR specific test was done every 2 weeks until day + 60 and then monthly until immunosuppression was over (in allogeneic setting). A PCR positive test triggered benznidazole treatment during 4 weeks. Medical records were reviewed looking for clinical signs suspected of CD. ECG and echocardiogram abnormalities were assessed.

Results: Twenty four pts/D (1.49%) were tested positive for CD. In the allogeneic setting 5 out of 457 (1.09%) pts and 5 out of 457 (1.09%) D with CD positive serology were found. Two D were also PCR positive and treated as mentioned before. Two out of 5 allogeneic pts. with positive serology developed a positive PCR on day +43 and +65 post HSCT and were successfully treated. Fourteen out of 690 autologous transplant pts were serologically positive and 4 of them had a positive PCR and treated. No reactivation was proved in the autologous setting.

Conclusions: 1.49% of the pts and D were tested as CD carriers. PCR test for CD is effective and safe detecting parasites allowing proper and timely effective treatment. Benznidazole was effective and no hematologic toxicity was related to this treatment. No pts diagnosed and treated developed parasitemia again. HSCT could be performed safely, despite profound and prolonged immunosuppression in pts with CD positive serology and also in those with circulating parasites if they were properly treated and monitored.

Cryopreserved vs Non-cryopreserved Graft Before Autologous Stem Cell Transplantation in Patients With Multiple Myeloma. A Comparative Study

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Introduction: Autologous Stem Cell Transplantation (ASCT) remains a standard first-line treatment in eligible patients with Multiple Myeloma (MM). Graft storage for a maximum of 72 hours at 2-6°C and infusion after high dose melphalan has been increasingly used and was adopted as an option for cryopreservation in our center in 2019.

Objectives: To compare time to neutrophil engraftment (>500/ul), time to platelets engraftment (>20000/ul), days of hospital stay, engraftment failure, one-year overall survival (OS), one-year relapse-free survival (RFS), one-year relapse rate, 100-days transplant-related mortality (TRM), MM response at 100 days after transplantation, number of red blood cell transfusions, and number of platelets transfusions, between patients that received an ASCT with cryopreserved graft and those who received a graft stored at 2-6°C (cryopreserved graft).

Materials and Methods: We conducted a retrospective comparative analysis of MM patients’ clinical records that received an ASCT in our center from January 2019 to April 2021. Cryopreserved grafts were stored in freezer at -80°C, DMSO and albumin were added as institutional protocol. Non-cryopreserved grafts were stored at 2-6°C for a maximum of 72 hours after collection. The conditioning regimen was melphalan 200/140 mg/m2 administered on day -2 with cryopreserved grafts and on day -1 with non-cryopreserved grafts. Kaplan-Meier curves were used for OS and RFS analysis and the long-Rank test was used for comparisons. The cumulative incidence function was used for TRM and relapse rate analysis.

Results: From January 2019 to April 2021, 88 patients (median age 56.9 years) with MM received an ASCT in our center. 47 (53.4%) received a cryopreserved graft and 41 (46.6%) received a non-cryopreserved graft. No statistically significant difference was found between groups regarding age, sex, MM status before ASCT, number of treatments before ASCT, ISS stage, time to transplant, CD34+ dose, plerixafor use, and renal function. Conditioning regimen was melphalan 200 mg/m2 in 79 (89%) and 140 mg/m2 in 9 (11%) patients. The median time from collection to graft infusion in non-cryopreserved grafts was 45.5 hours. No statistically significant difference was found between groups with regard to time to neutrophil and platelets engraftment, number of red blood cell and platelets transfusions, OS, RFS, relapse rate, TRM, and MM response after transplant. There were no graft failure events. Patients receiving a non-cryopreserved graft had a shorter hospital stay (14 vs 15 days; p=0.008).

Conclusion: ASCT with non-cryopreserved graft in MM patients showed similar results to the cryopreserved modality, with a shorter hospital stay and avoiding DMSO potential toxicity.

Table 1. ASCT with cryopreserved and non-cryopreserved graft outcomes (n=88)

<table>
<thead>
<tr>
<th></th>
<th>Cryopreserved</th>
<th>Non-cryopreserved</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days Neutrophil Engraftment, Median (IQR)</td>
<td>11 (11-12)</td>
<td>11 (11-12)</td>
<td>0.957</td>
</tr>
<tr>
<td>Days Platelets Engraftment, Median (IQR)</td>
<td>12 (11-13)</td>
<td>12 (11-13)</td>
<td>0.946</td>
</tr>
<tr>
<td>OS 1y, % (95%CI)</td>
<td>98 (85-99)</td>
<td>90 (74-98)</td>
<td>0.894</td>
</tr>
<tr>
<td>RFS 1y, % (95%CI)</td>
<td>79 (81-89)</td>
<td>78 (59-91)</td>
<td>0.814</td>
</tr>
<tr>
<td>Relapse Rate 1y, % (95%CI)</td>
<td>22 (10-38)</td>
<td>22 (7-43)</td>
<td>0.549</td>
</tr>
<tr>
<td>100-days TRM 1y, % (95%CI)</td>
<td>2 (0-2.10)</td>
<td>0</td>
<td>0.337</td>
</tr>
<tr>
<td>Red Blood Cells Transfusions, mean (SD)</td>
<td>0.49 (0.9)</td>
<td>0.3 (0.5)</td>
<td>0.232</td>
</tr>
<tr>
<td>Platelets Transfusions, mean (SD)</td>
<td>4 (4.8)</td>
<td>5 (4.7)</td>
<td>0.420</td>
</tr>
<tr>
<td>Days of Hospital Stay, median (IQR)</td>
<td>15 (14-16)</td>
<td>14 (13-15)</td>
<td>0.008</td>
</tr>
</tbody>
</table>
Hematopoietic Cell Transplantation From Volunteer Unrelated Donor Between 2016 and 2021: A Collaborative Study GATMO-TC and INCUCAI

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Introduction: Hematopoietic cell transplantation (HCT) from HLA-matched (MUD) or HLA-mismatched unrelated donors (MMUD) offers a curative strategy for patients with many malignant and benign hematological diseases. However, the success of HCT may be limited because of graft versus host disease, graft failure, and relapse disease. We aimed to describe donor’s and recipient’s features, and their association with survival, for patients who underwent a MUD and MMUD in Argentina between 2016 and 2021.

Methods: We used data from a national database (SINTRA) for HCT managed by Instituto Nacional Central Único Coordinador de Ablación (INCUCAI). All transplant centers are affiliated to Grupo Argentino de Trasplante de Médula Ósea y Terapia Celular (GATMO-TC). Only a first HCT with a volunteer unrelated donor was included, both MUD and MMUD using high-resolution HLA. Patients who underwent transplants with umbilical cord blood (UCB) were excluded. Overall survival (OS) was estimated by Kaplan-Meier curves and compared by log-rank test.

Results: A total of 617 cases (median age 18 years; range 0.5-73; 287 cases less than 18 years old) were included: 2016 n=80, 2017 n=97, 2018 n=116, 2019 n=134, 2020 n=84, y 2021 n=106. Main diagnostics were: acute lymphoblastic leukemia (ALL) n=161, acute myeloblastic leukemia (AML) n=125, myelodysplastic syndrome (MDS) n=88, immunodeficiencies n=74, aplastic anemia n=53, myeloproliferative neoplasms (MPN) n=29, and non-Hodgkin lymphoma n=19. In the group of patients less than 16 years old, the more frequent diagnosis was ALL (33%) followed by immunodeficiencies (24%); in patients older than 16 years old, AML (27%) and MDS/MPN (25%). Stem cell source was peripheral blood in 473 cases (77%). Considering four HLA-locus studied, donors were 6/8 n=4, 7/8 n=254, and 8/8 n=357. By considering also DQB1, the donors were 8/10 n=13, 9/10 n=344 (13 with DQB1 mismatched), and 10/10 n=344. Donors (median age 30 years) were from: Germany n=224, Argentina n=140, EEUU n=90, Brazil n=42, Poland n=25, Israel n=18, Spain n=14, Great Britain n=11, Chile n=9, Italy n=9, Switzerland n=7, Turkey n=7, Portugal n=6, France n=4, The Netherlands n=3, Austria n=1, Canada n=1, China n=1, Sweden n=1, Thailand n=1. The proportion of Argentinian donors was increasing along the calendar year since 10% in 2016 to 28% in 2021. Median of follow-up for the surviving cohort was 365 days (IQR 176-730). One-year OS was 66% (95%CI 62-70). No difference was found in terms of OS regarding age and sex recipient, donor/recipient sex matching, benign and malignant diseases, stem cell source, and between MMUD and MUD (Fig1).

Conclusions: HCT with a volunteer unrelated donor is a feasible treatment in our country, even considering mismatched donors. A third of donors were coming from Argentina highlighting the role of the national donor’s registry in our country.
Co-transplantation With Adipose Tissue-Derived Stem Cells Improves Engraftment of Transplanted Hepatocytes

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Background: Hepatocyte transplantation is expected to be an alternative therapy to liver transplantation. However, poor engraftment is a severe obstacle to be overcome. The adipose tissue-derived stem cells (ADSCs) are known to secrete various factors to provide a growing environment, and improve engraftment of transplanted pancreatic islets, which have many similarities to the hepatocytes. Therefore, we examined the effects and underlying mechanisms of ADSC co-transplantation on hepatocyte engraftment.

Methods: Hepatocytes and ADSCs were obtained from F344 rat. In a study of in vivo model, the analbuminemic rats which are syngeneic to donor rats were used as recipient rats, and the serum albumin levels were quantified to evaluate the hepatocyte engraftment. To examine the effect of ADSC co-transplantation, hepatocytes and ADSCs were co-transplanted into the renal subcapsular space and liver. Hepatocytes and ADSCs were separately transplanted into the right and left renal subcapsular space to investigate the effect of the proximity between both cells. In transplantation into the liver, fluorescent staining to trace transplanted cells in the liver were also performed. To identify the factors that promote the engraftment, an in vitro study was performed. The ammonia metabolic assay was analyzed to examine the effect of ADSC co-culture on hepatocyte function. The co-cultured supernatants were analyzed by a multiplex assay to identify the factors which are secreted by ADSC, and inhibition test using neutralizing antibodies for target factors was also performed.

Results: The serum albumin levels in the renal subcapsular space and liver (Figure 1) were significantly higher in the case of co-transplantation with ADSCs (p<0.001, p<0.001). In the separately transplantation model, the serum albumin levels were significantly decreased, suggesting that close proximity between hepatocytes and ADSCs was necessary to exert this effect. Also, in the transplantation into the liver, approximately 50% of transplanted hepatocytes were attached and the inhibition test demonstrated that the neutralizing antibodies for above three factors suppress the abovementioned effects of ADSCs (Figure 2).

Conclusion: The present study revealed that ADSC co-transplantation can improve the engraftment of transplanted hepatocytes. This effect was only seen when ADSCs and hepatocytes were in close proximity, and may be based on crucial factors, such as HGF, VEGF, and IL-6, which are secreted by ADSCs.
Humanized Mouse Models Are Misleading to Evaluate CARTreg Function

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Introduction: Chimeric antigen receptors CARs can be used to change the specificity of FOXP3+ regulatory T cells (Tregs) for the induction of tissue specific tolerance. We and others have shown that CAR-Tregs specific for transplant mismatched HLA-A*0201 (A2-CAR) can be used for tolerance induction in humanized mouse models.

Methods: We now wanted to study the therapeutic potential of MHC-specific CAR Tregs in an immunogenic, non-lymphopenic mouse model. To this end, we generated H-2Kb-specific scFv from phage display libraries to create second generation CARs with a CD28/CD3z signaling domain.

Results: The CARs showed good surface expression and strong activation of Tregs with an exclusive Kb-specificity. They were much more effective in suppression of CD4+ and CD8+ effector T cells in allogeneic mixed lymphocyte reaction as compared to nTregs. Kb-CAR-Tregs prevented skin transplant rejection in BALB/c RAG1-/- after cotransfer with equal numbers of effector T cells. To our major surprise adoptive transfer of CAR-Tregs in an immunogenic C57BL/6 to BALB/c skin transplant did not result in any meaningful prolongation of transplant survival in a non-lymphopenic setting. We therefore cloned our anti-MHC*0201 scFv from the initial experiments in our humanized mouse models into a murine CAR vector. However, the rejection of A2-transgenic C57BL/6 skin grafts into C57BL/6 recipients (single MHC mismatch) was also not prolonged with adoptive transfer of A2-CAR Tregs. Although lymphodepletion and rapamycin prolonged graft survival, the addition of Kb-CAR Tregs had no added benefit, although we observed long-term persistence of CAR-Tregs and a strong accumulation of the transferred Tregs within the graft. In fact, the transferred CAR-Tregs made up to 40% of all intragraft Tregs ruling out too small local Treg numbers as the reason for the low in vivo efficiency.

Conclusion: Weakly immunogenic humanized mouse models can be misleading to evaluate the effectivity of CAR-Tregs for clinical translation. Lymphodepleting strategies strongly increase the accumulation of graft-specific Tregs within the grafts. In order to develop clinically meaningful protocols for CAR-Treg therapies more immunogenic, non-lymphopenic models are required.

Genetic Identity Evaluation in Human Cell Cultures for Clinical Research/Cell Therapies: Comparison of Two Molecular Methods

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Introduction: Cell therapies are a constantly growing field of research, with benefits documented for numerous conditions in clinical and pre-clinical studies. Within these studies, cell expansion or cell culture is often needed. Cell line contamination and misidentification is a significant threat facing cell culture, with the potential to invalidate resulting data. To avoid misidentification in Human cell lines for research, performing short tandem repeat (STR) profiling is recommended. However, for cell therapies products guidance only states that testing procedures should be implemented to ensure cell cultures identity and that acceptable limits for culture composition should be defined. The National Public Umbilical Cord Blood Bank of the Garrahan Pediatric Hospital (BSCU) executes quality control of the manufacturing process as well as the final product according to national and international standards and regulations. HLA typing, by means of PCR Sequence-Specific Oligonucleotide (SSO) technique (LABType One Lambda), is commonly used in many laboratories to asses compatibility for transplantation, including ours. HLA genes are highly polymorphic, hence we aimed to study whether HLA typing by SSO-PCR could be used as a method to assess genetic identity in cell cultures intended for cell therapies.

Method: DNA samples (5) were obtained from HSC of 4 umbilical cord blood and 1 peripheral blood from the mother of one of them after Informed Consents were signed. Mixed DNA serial dilutions (1:10; 1:25; 1:50) were analyzed for genetic identity by both molecular methods. STR (AmpFLSTR identifier Plus, Applied Biosystems) was performed according to manufacturer’s protocols and PCR-SSO technique (LABType One Lambda) was performed according to SOP.

Results: Unique DNA profiles were obtained for each sample with both methods. For the DNA mixtures, we were able to detect contamination in all the conditions (100%) analyzed by STR profiling. However, HLA typing showed different results depending on the gene analyzed (Table 1). HLA typing by STR was able to detect all of the contaminated samples, despite the contamination levels. Since the scientific/clinic community is yet to determine which is the degree of cross-contamination of a culture that could negatively influence cell therapy or clinical research, both techniques could be used depending on each laboratory capabilities.

Table 1: Percentage of samples with detected cross contamination, according to the technique and gene analyzed.
Expression of Traf2- And Nck-Interacting Kinase in EMT-inhibited Human Amniotic Epithelial Cells

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Introduction: The human amniotic epithelial cell (hAEC), a type of placental stem cell, has been investigated as a new source of regenerative therapy. We previously demonstrated that the hAECs underwent TGF-β-dependent epithelial-mesenchymal transition (EMT) shortly after starting cell culture, which was sufficiently inhibited by a TGF-β pathway inhibitor, SB-431542. Using comprehensive transcriptome analysis, we found a differentially expressed gene, Traf2- and Nck-interacting kinase (TNIK) significantly enriched in SB-431542-treated hAECs. TNIK is a member of the germinal center kinase family and is ubiquitously expressed with a high level in the brain and small intestine, but low in the placenta. It has been reported that TNIK plays an important role in the regulation of Jun N-terminal kinase pathway activation and cytoskeletal rearrangements. Additionally, TNIK phosphorylates the T-cell factor-4 (TCF4) and is also known as an important activator of the Wnt pathway. In this study, we explored the role of TNIK in hAECs.

Methods: hAECs were isolated from the placentae of 6 patients who underwent Caesarean sections. The cells were cultured for 7 days with or without SB-431542. Total RNA was extracted on day 0 (naïve cell), day 1, 4, and 7, and then the expressions of TNIK were analyzed by RT-qPCR. Additionally, we cultured the hAECs with supplementation of a TNIK inhibitor, NCB-0846, which binds to TNIK in an inactive conformation and inhibits the phosphorylation of TCF4, and examined the cell proliferation.

Results: We confirmed that TNIK was significantly expressed in cultured hAECs with SB-431542 for 7 days by RT-qPCR. TNIK was not observed in naïve hAECs but gradually expressed in inhibited-EMT hAECs over days. The supplementation of NCB-0846 influenced cell viability and proliferation.

Conclusions: Our data showed that the TNIK expression in hAECs was induced by inhibition of TGF-β-dependent EMT. The blocking TNIK/TCF4 interaction using NCB-0846 interfered with cell proliferation. Further study is needed to clarify the crosstalk between TGF-β and Wnt pathways in hAECs. Regulation of these signaling pathways might be useful to develop a clinical protocol for cell transplantation therapy using hAECs.
4-Octyl Itaconate Inhibits Hypoxia-Induced Injuries on β-cell Via Reducing LDHA-Mediated ROS Generation

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Introduction: Islet transplantation has been shown as a potential way to cure Type 1 Diabetes. However, isolation and purification inevitably devascularize the islets. Hypoxia stress has been observed up to 60% of newly transplanted tissue during the first couple of days which increase the hypoxia induced β-cell death. Reactive oxygen species (ROS) are key factors mediating hypoxic damage in β-cell and are mainly generated in NADPH or NADH dependent pathways. Itaconate is a by-product of the tricarboxylic acid cycle that protects cell from inflammation and oxidative stress induced damage. However, the effect of itaconate for β-cell in hypoxia condition still unknown. In this study, we aimed to explore the effect of 4-OI, a cell-permeable derivative of itaconate, on protection beta cells from hypoxia-induced damage and its mechanism.

Method: MIN6 cells were cultured under hypoxic conditions (1% O2) with or without 125μM 4-Ol in vitro for 72h. The viability of cells was examined using MTS assays and flow cytometric analysis. The levels of inflammatory cytokines were detected by qRT-PCR and ELISA assays. Intracellular ROS content was measured by DCFH-DA probe. LDH activity assay kit was used to test the activity of LDHA. Finally, cells were treated with ROS scavenger N-acetylcysteine (NAC) and LDHA specific inhibitor FX-11 in hypoxia condition for 72h to verify the role of 4-OI in regulating ROS.

Results: Hypoxia-induced injuries on MIN6 cells were confirmed by decreased cell viability, increased oxidative stress and apoptosis, and the production of inflammatory cytokines when compared with normoxia. After the treatment of 4-OI, those changes caused by hypoxia injury were effectively reversed. The viability of MIN6 cells under hypoxia was improved, the intracellular ROS level, inflammatory cytokines and apoptosis were decreased. Similarly, when we used ROS scavenger NAC to treat the cells with hypoxia, cell viability was increased while the quantity of intracellular ROS, and inflammatory cytokines were reduced. Then, we found that the level of NADPH was not significantly altered under hypoxia, whereas NADH was dramatically increased. When the cells treated with 4-OI, the level of NADH was down-regulated. In addition, we found that 4-OI decreased LDHA activity, which suggested the production of ROS triggered the cell death was from the interaction of LDHA and NADH. Finally, to confirm our findings, we treated hypoxic cells with FX-11, a specific inhibitor of LDHA. The treatment of FX-11 enhanced cell survival, inhibited the production of ROS, and reduced the level of inflammatory cytokines.

Conclusion: In this study, we provide evidence that 4-OI can decrease the interaction of LDHA-NADH then reduce the generation of ROS which finally protect the β cell under hypoxia condition.

Natural Science Foundation of Hunan Province, China (Grant No.:2021JJ31018).
Is There Any Role of Combined Use of Gene Expression Profiling and Donor Derived Cell Free DNA in Worsening Renal Allograft Function

Introduction: There are multiple noninvasive tests available to assess risk of renal allograft rejection. Donor-derived cell-free DNA (dd cf DNA) test is used to assess rejection in the settings of worsening renal allograft function while Gene profiling is used to assess the subclinical rejection in the settings of stable graft function. OmniGraf™ is a combination of Gene profiling and dd cf DNA tests and used for diagnosing possible subclinical rejection in the settings of stable renal allograft function. But not much has been observed in the settings of worsening renal allograft function. Here we are presenting our study aiming to correlate OmniGraf™ result with the biopsy outcomes.

Methods: We selected 40 patients who had a biopsy either for cause or for protocol along with OmniGraf™ and serum creatinine checked around the same time of the biopsy. Patients were divided into 2 major groups, 1. protocol, and 2. For-cause biopsy, later subdivided into 4 groups depending on the OmniGraf™ result combinations. TX is considered No Rejection, Non-TX is considered increased risk of subclinical rejection.

Result: In the protocol biopsy group 12 out of 19 patients who had TX with normal TRAC had rejection on the biopsy. The normal result of OmniGraf™ TX with normal TRAC was supposed to predict no rejection, so if biopsy was not performed it might have missed 57% of rejection. This suggests that Non-TX is not a risk factor for TRAC level is good in predicting possible rejection, irrespective of the type of rejection.

In the for-cause biopsy group, the subgroup 2 of 2 patients with TX and normal TRAC had rejection on biopsy. The normal result of OmniGraf™ is not reliable to rule out rejection. The subgroup TX with high TRAC is good in capturing rejection for 6 out of 6 patients. This suggests that TX may not be useful in this group in predicting rejection as dd cf DNA test, alone might have been able to predict the rejection. The subgroup Non-TX with normal TRAC is showing 37.5% patients, positive for rejection on biopsy while Gene profiling is used to assess the subclinical rejection in the settings of stable graft function. Our data are limited to suggest clinical or statistical relevance. It is probably more useful in serial monitoring of OmniGraf™ than one single value to capture subclinical rejection. Our data are limited to suggest clinical or statistical relevance. It would be useful to evaluate these results on a larger scale to understand the usefulness of this test in kidney transplant recipients with worsening renal allograft function.

<table>
<thead>
<tr>
<th>PROTOCOL BIOPSY</th>
<th>FOR CAUSE BIOPSY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acute Rejection</td>
</tr>
<tr>
<td>Acute Rejection</td>
<td>5</td>
</tr>
<tr>
<td>NO Rejection</td>
<td>3</td>
</tr>
</tbody>
</table>

| TRAC             | Acute Rejection | NO Rejection |
|------------------|-----------------|
| Normal TRAC      | 3               | 4            |
| TX with Normal TRAC | 1               | 2            |
| TX with High TRAC | 0               | 0            |
| Non TX with Non TRAC | 0               | 2            |
| Non TX with High TRAC | 0               | 0            |
Kidney Graft Resistance Index, Its Association With Vascular Patterns and Kidney Function Assessment After 2 Years

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Introduction: Kidney graft resistance index (RI) measured by vascular Doppler sonography has been associated with systemic and local vascular factors with negative effects on the kidney function evolution, which is why RI may be a prognostic factor of graft function.

Objectives: To determine the relation between RI and factors influencing the graft function, and whether there is an association between increased RI and a worsened evolution of kidney function.

Methods: Vascular Doppler ultrasound was performed in 119 stable living- and deceased-donor renal transplant patients more than 3 months after transplantation. Their RI was measured initially at a check-up (T0) and then two years later (T1). RI was analyzed in a bimodal way (RI <0.8 and ≥0.8) and by tertiles (<0.68, 0.69-0.81, >0.81). Creatinine (Cr), glomerular filtration (GF) using the CKD-EPI equation, and proteinuria were also assessed upon measuring RI: (T0) and after 2 years (T1). The relationship with other variables, such as age, diabetes (DM), delayed graft function (DGF), was analyzed and, during those two years, the presence of rejection, recurrent urinary tract infections (rUTIs) and progression to dialysis or death was described.

Results: Male 44%; average age 48 years (38-57); DM 17%; DGF 59%. Kidney function at T0 was: Cr 1.3 (1.1-1.7), GF 54 (40-65), proteinuria 0.22 (0.14-0.4) and at T1: Cr 1.31 (1.07-1.7), GF 56 (40.3-69.8), proteinuria 0.24 (0.14-0.4). Progression to death 8%, dialysis 9%, rejection 8%, UTI 8%. The bimodal analysis showed a significant relation between RI >0.8 and older age (p=0.001) and DM (P=0.004). The tertile analysis indicated a significant relation with older age (p=0.001), increasing when comparing tertiles <0.68 and >0.81 (p=0.0001). There was also a significant association between DM and the highest RI tertile (p=0.01). Both the bimodal and the tertile analyses showed increased Cr levels and decreased GF rates in RI >0.8, but no significant relation. There was no significant difference in Cr, GF and proteinuria between T0 and T1 either. There was no relation with sex, DGF, progression to death, dialysis, rUTI or rejection.

Conclusion: An association between increased RI and older age and DM, as reported in other studies, is found. Such variables are directly related to vascular factors, such as increased pulse pressure and microvascular injury, elements known to impair graft function in the long term. Even though this study shows a tendency to a worsened kidney function with a high RI, its relation is not significant and no difference is found after 2 years. Further studies with greater time variation are required to assess these parameters.
Comparative Analysis of Perioperative Complications in Kidney Transplant Patients With Coronary Artery Disease on Dual Antiplatelet Therapy (DAPT)

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Introduction: Antiplatelet drugs cannot be stopped at the time of transplantation in some recipients with coronary artery disease (CAD). This may increase peri-operative bleeding. We have analyzed our experience.

Methods: We retrospectively analyzed data of recipients with CAD, taking DAPT (Clopidogrel 75 mg and Acetylsalicylic acid 150 mg). Based on pre-operative evaluation by cardiologist, patients were segregated into two groups: Group-A (drugs discontinued 5 days prior to procedure), Group-B (drugs continued, because of high risk of acute coronary event, on discontinuation). Both groups were analyzed with respect to age, body mass index, pre and postoperative hemoglobin (post-operative day one), intra-operative blood loss, drain output (DO), need for blood transfusion (BT), bleeding complications (need for any intervention), any cardiovascular event upto one month follow-up. Continuous variables were compared using Mann Whitney-U test and dichotomous variables analyzed using Chi-Square test, p-value of 0.05 considered significant.

Results: From December 2014 to January 2021, 106 patients were identified, (Group A = 73, Group B = 33). These groups were comparable in terms of all the listed parameters except significantly higher DO in Group B, Table 1. No adverse cardiovascular event was noted. No patient required any intervention for bleeding.

Conclusions: With proper attention to intra-operative hemostasis, transplants can be performed safely in patients on DAPT.

**TABLE 1.** Peri-operative parameters.

<table>
<thead>
<tr>
<th>A</th>
<th>Blood loss (ml)</th>
<th>Drain output (ml)</th>
<th>Blood transfusion</th>
</tr>
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<tbody>
<tr>
<td>290(260-330)</td>
<td>220(196.32-244.35)</td>
<td>24/73</td>
<td></td>
</tr>
<tr>
<td>280(270-310)</td>
<td>330(301.60-358.26)</td>
<td>8/33</td>
<td></td>
</tr>
</tbody>
</table>

@: Median + Interquartile range; *: Chi Square; **: Mann Whitney U.

Influence of CYP3A5 Polymorphisms on Tacrolimus Dosing in Renal Transplant Recipients

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Introduction: Tacrolimus is a commonly used immunosuppressant after kidney transplantation it has narrow therapeutic range and demonstrates wide interindividual variability in pharmacokinetics leading to potential under immunosuppression or tacrolimus toxicity genetic polymorphism in CYP3A5 enzyme expression contributes to differences in tacrolimus bioavailability between individuals.

Aim of the study: Ti evaluate pharmacogenomic effect of CYP3A5 gene polymorphisms on tacrolimus dosing in renal transplant recipients.

Materials and Methods: Present study we investigated pharmacogenomics associations of common CYP3A5 polymorphisms with requirements of tacrolimus in renal transplant patients:

**INCLUSION CRITERIA** - 50 patients on tacrolimus based triple immunosuppression were genotyped for cyp3A5 polymorphism most alleles ^1/*1,^1/*3,^3/*3 alleles.

**EXCLUSION CRITERIA**- those patients on CYP inducers or inhibitors were excluded demographic data, weight based tacrolimus doses, serum tacrolimus level at 1 month, 3 months 1 year and present tacrolimus trough level were collected.

Data was statistically analysed.

Results: Mean age of the recipients was 33.41+-10.2,72% were males mean tacrolimus level at 1 month was 8ng/ml (7-10ng/ml) at 1 month post transplant cyp ^1/*1 was 5.75+_0.95,tac level in cyp3a5 ^1/*3 was 9.52+_1.42,CYP3A5^3/*3 -10.26+_1.02 with significant P VALUE <0.01 among patients with high tac level 36% were poor metabolisers,50% intermediate metabolizers,none of the extensive metabolisers had higher tacrolimus level. At>3 months of transplantation tac level in cyp3a5 ^1/*1 was 5.75+0.95, cyp3a5 ^1/*3 was 6.33+_1.17, cyp3a5 ^3/*3 was 6.78+_0.8 with significant P value < 0.01. 56% developed tac toxicity - 84%(*3/*3) poor metabolisers, 14.3% in intermediate ^1/*3 metabolisers,125 developed rejections in first three months of transplant,90.755 were extensive metabolisers.

Discussion: Tacrolimus toxicity as well as rejection due to sub therapeuic levels influence graft outcomes; bioavailability of tacrolimus varies widely due to gene polymorphisms of CYP3A5 gene. CYP3A5^1/*1 had lower tac level in blood resulting higher rates of rejection requiring 1.5 to 2 times higher dose compared to poor metabolisers and intermediate metabolizers. Poor metabolizers ^3/*3 had tacrolimus related toxicity at similar dose adjusted tac levels, indicating lower dose for maintenance (0.06mg/kg).

Conclusion: Genotyped based dosing may improve achievement of therapeutically drug concentrations with reduced drug related complications in the era of personalised medicine.
The Impact of Dialysis Vintage on Cardiovascular Risk Factors And the Findings of Cardiovascular Screening Work Up of Renal Transplant Candidates

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Methods: In a single center retrospective chart-review study, we reviewed the outcomes renal transplant recipients who underwent renal transplant from January 2017 to May 2020. We divided the group based on their dialysis vintage, less than 3 years versus more than 3 years. We collected the data about the patients' demographics, cardiovascular risk factor, dialysis modality, pre-transplant work-up images, and the changes in cardiovascular risk factors in the first post-transplantation year.

Results: We included 278 patients, 109 patients in the longer vintage group and 169 patients in the shorter vintage group. The mean age 43.8±16.1 and 164 patients (59%) were male. The mean dialysis vintage in the shorter group was 1±0.1 year, and 5.7±2.7 years in the longer vintage group, p <0.001. The most common comorbidities were hypertension (76%), followed by diabetes mellitus (41.7%), and were present in similar proportions of both groups. Compared to the shorter dialysis vintage group, those who had longer dialysis vintage were more likely to have a deceased kidney donor (36.7% vs 8.9%, p <0.001), receive hemodialysis (88.1% vs 76%; p=0.006), predominantly through an arteriovenous fistula (55% vs 20.7%; p <0.001). The results of pretransplant work up including cardiac stress test, calcium scoring, coronary angiogram, cardiac ejection fraction, left ventricular hypertrophy, wall motion abnormalities and the degree of calcifications of pelvic arteries on pelvic Ct scan did not differ between the two groups. In the first post-transplantation year, patients in the longer vintage group were more likely to have a deceased kidney donor (36.7% vs 8.9%, p <0.001), receive hemodialysis (88.1% vs 76%; p=0.006), predominantly through an arteriovenous fistula (55% vs 20.7%; p <0.001). The results of pretransplant work up including cardiac stress test, calcium scoring, coronary angiogram, cardiac ejection fraction, left ventricular hypertrophy, wall motion abnormalities and the degree of calcifications of pelvic arteries on pelvic Ct scan did not differ between the two groups. In the first post-transplantation year, patients in the longer vintage group were more likely to have a deceased kidney donor (36.7% vs 8.9%, p <0.001), receive hemodialysis (88.1% vs 76%; p=0.006), predominantly through an arteriovenous fistula (55% vs 20.7%; p <0.001). The results of pretransplant work up including cardiac stress test, calcium scoring, coronary angiogram, cardiac ejection fraction, left ventricular hypertrophy, wall motion abnormalities and the degree of calcifications of pelvic arteries on pelvic Ct scan did not differ between the two groups. In the first post-transplantation year, patients in the longer vintage group were more likely to have a deceased kidney donor (36.7% vs 8.9%, p <0.001), receive hemodialysis (88.1% vs 76%; p=0.006), predominantly through an arteriovenous fistula (55% vs 20.7%; p <0.001). The results of pretransplant work up including cardiac stress test, calcium scoring, coronary angiogram, cardiac ejection fraction, left ventricular hypertrophy, wall motion abnormalities and the degree of calcifications of pelvic arteries on pelvic Ct scan did not differ between the two groups. In the first post-transplantation year, patients in the longer vintage group were more likely to have a deceased kidney donor (36.7% vs 8.9%, p <0.001), receive hemodialysis (88.1% vs 76%; p=0.006), predominantly through an arteriovenous fistula (55% vs 20.7%; p <0.001).

Conclusions: Our study showed that patients with dialysis vintage up to 3 years were not different in their baseline traditional risk factors, cardiovascular pre-transplant work up, nor the changes post renal transplant. This suggest that the increase of mortality related to dialysis vintage might be related to other factors such as uremia, electrolytes shifts and/ or infections. Further studies with longer follow up are needed to investigate if dialysis vintage longer than three years would affect the pre-transplant cardiovascular risk factors or the findings of pre-transplant cardiovascular imagings.

Do the Findings of Pre-transplant Cardiovascular Imaging Corollate With Having Persistent Hyperparathyroidism at Year Post Renal Transplantation?

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Background: Hyperparathyroidism is common in chronic kidney disease, and it can persist post renal transplantation. It is unknown whether the findings of cardiovascular imaging pre-transplantation corollate with the persistence of hyperparathyroidism (pHPTH) at one-year post-renal transplantation.

Method: A single center retrospective study of renal transplant candidates from January 2017 to May 2020. We collected patients' demographics, cardiovascular risk factors, the findings of pre-transplant cardiovascular imaging (echo, nuclear cardiac perfusion stress test, calcium scoring, cardiac catheterization results and the degree of calcification/atherosclerosis of pelvic arteries on screening pelvic CT scan). We also collected iPTH values [at baseline (before transplant), 1-6 months, 6-12 months, and 12-24 months post transplantation]. We defined pHPTH as iPTH ≥25.5 pmol/L after 12 months post kidney transplantation (normal=12.73 pmol/L).

Results: 287 renal transplant recipients were included. 74% were ≥30 years, 58% were men and 80% were living-donor kidney recipients. Preemptive transplantation was 10.1%, PD: 11.5% and HD: 78.4% (AVF: 42% versus Permcath: 58%). Dialysis vintage was 4.8±3.3 years for deceased donor kidney transplantation (DDKT) versus 2.4±2.6 years for living donor kidney transplantation (LKT). The prevalence of pHPTH was [n=47 (16.4%)]. There were no association between pHPTH and the findings of pre-transplant cardiovascular imaging including echo findings (EF, LVH and abnormal wall motion), cardiac nuclear perfusion stress test (cardiac PET), cardiac catheterization, calcification/atherosclerosis of pelvic arteries seen on screening pelvic CT scan. However, the presence of calcium scoring ≥400 on pre-transplant cardiac PET scan was associated with higher incidence of pHPTH at 12 months post renal transplantation (57% versus 13%; P: 0.013).

Conclusion: There was no association between the incidence of pHPTH post-renal transplant and pre-transplant cardiovascular imaging. However, higher calcium scoring PET scan (>400) are associated with higher incidence of pHPTH at 12 months post renal transplantation.
Pregnancy in Renal Transplant Recipients: Long Term Outcomes

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Introduction: Kidney transplantation is considered the method of choice in the treatment of end-stage chronic kidney disease. It improves patient survival and quality of life, including the recovery of fertility amongst women, posibilisitng pregnancy.

Aim of study: Describe a single center experience with pregnancy after transplantation on its epidemiology, its frequency in women in their reproductive years, outcomes for the mother and newborn, and compare patient and graft survival with a matched control group of women who did not get pregnant during the study period.

Materials and Methods: Retrospective case-control study, developed at the Kidney Transplant Service of Santa Casa de Misericórdia in Porto Alegre, among the 1253 female patients who, after transplantation, were of childbearing age in the period 1977 to 2016, followed up until the end of 2020. These were compared to a control group matched for age, type of donor, date of transplant and immunological risk.

Results: A total of 76 (6.1%) of the patients were pregnant, totaling 93 pregnancies. Compared to the control group, at 10 years after transplantation there was no significant difference in relation to graft loss (74% vs 66%, p=0.524) but the survival of pregnant patients was higher (97% vs 79%, p=0.018). We observed that a total of 40% of pregnancies progressed to abortion. In 30% the delivery was preterm and 26% were born at term. Three pregnancies progressed to stillbirth. Of the 56 pregnancies that evolved, 23 (41%) had preeclampsia and one eclampsia.

Conclusion: 6.1% of women of childbearing age became pregnant during the studied period, 56% of pregnancies were successful. Compared to the control group, pregnant women had similar graft survival and longer patient survival.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pregnant n=76</th>
<th>Control n=76</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at transplant (SD)</td>
<td>23.81(7.29)</td>
<td>25.45(6.91)</td>
</tr>
<tr>
<td>Live donor (%)</td>
<td>52 (68)</td>
<td>52 (68)</td>
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<tr>
<td>Fist Transplant</td>
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<td>Diabetes</td>
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<td>1</td>
</tr>
<tr>
<td>Donor specific antibodies</td>
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<td>3</td>
</tr>
<tr>
<td>Induction therapy (depleting)</td>
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</table>

Maintenance Immunosuppression

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<th>Drug</th>
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<th>Control n=76</th>
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</thead>
<tbody>
<tr>
<td>Azathioprine</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Mycophenolate acid</td>
<td>16</td>
<td>22</td>
</tr>
<tr>
<td>Ciclosporine</td>
<td>39</td>
<td>41</td>
</tr>
<tr>
<td>Tacrolimus</td>
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<td>19</td>
</tr>
<tr>
<td>Steroids</td>
<td>72</td>
<td>74</td>
</tr>
<tr>
<td>ImTOR</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>1977-1999</td>
<td>40</td>
<td>42</td>
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<tr>
<td>2000-2016</td>
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Values are presented as median (range) unless otherwise noted.

Pregnancy (n=93)

<table>
<thead>
<tr>
<th>Pregnancy outcome n (%)</th>
<th>Live births</th>
<th>Miscarriage</th>
<th>Therapeutic terminations</th>
<th>Stillbirth</th>
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<tr>
<td></td>
<td>52 (56)</td>
<td>19 (20)</td>
<td>19 (20)</td>
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</table>

<table>
<thead>
<tr>
<th>Pregnancy outcome n (%)</th>
<th>Birth weight of infant (g)</th>
<th>Post-pregnancy graft rejection, n (%)</th>
<th>2-years post-pregnancy graft loss, n (%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>2400 (1923 – 2750)</td>
<td>11 (15)†</td>
<td>13 (14)</td>
</tr>
</tbody>
</table>

†n=76
A Noninferiority, Randomized Controlled Trial of Late Conversion to Once-Daily Regimen of Sirolimus and Extended-Release Tacrolimus Versus Mycophenolic Acid and Extended-Release Tacrolimus for Kidney Transplant Recipients (ODKT Trial)

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Background: Once daily immunosuppressive regimen could improve medical adherence and quality of life of kidney transplant recipients. Sirolimus based regimens can reduce calcineurin inhibitor (CNI) exposure. Therefore, we conducted randomized controlled trial, comparing once daily regimen of sirolimus and extended-release tacrolimus (ER-Tac) versus standard regimen of mycophenolic acid (MPA) and ER-Tac for late conversion in low immunologic risk kidney transplant recipients.

Methods: This randomized controlled, open label, noninferiority trial was conducted from April 2018 to March 2022 at King Chulalongkorn Memorial Hospital and Ehmirimajangarinda Kidney Institute Hospital, Thailand. The low immunologic risk renal transplant recipients greater than 4-month post transplantation were randomized 2:1 to once daily arm and standard arm. The once daily arm was sirolimus and ER-Tac compared with the standard arm, MPA and ER-Tac. The target level of sirolimus and ER-Tac were 6-10 ng/ml and 2-4 ng/ml, respectively. While 4-7 ng/ml of tacrolimus level was the goal trough level for standard regimen. Patients were followed up for 12 months.

Results: Seventy-two kidney transplant recipients were randomized to once daily arm (n = 48) or standard arm (n = 24). The baseline characteristics of patients were comparable both groups. The primary endpoint, mean eGFR at 12 months was 74.75 ml/min/1.73m^2 in once daily group and 70.5 ml/min/1.73m^2 in standard group, respectively. There were no biopsy-proven acute rejection and specific antibody and protocol kidney biopsy were followed up at 12 months.

Conclusion: Once daily regimen of sirolimus and ER-Tac was noninferior to standard regimen for mean eGFR at 12-month after conversion in low immunologic risk kidney transplant recipients. The Kidney Foundation of Thailand. The Royal College of Physicians of Thailand. The Kidney Foundation of Thailand.

The Outcome of the Inferior Epigastric Artery as a Donor Vessel for Managing Accessory Renal Arteries in Renal Transplantation: A Systematic Review and Meta-Analysis

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Background: Utilisation of renal allografts with multiple renal arteries (MRA) has always been considered a technical challenge during implantation of renal allografts. There is sparse literature comparing the implantation technique of MRA and allograft outcomes. The aim of this study was to perform systematic review and meta-analysis of literature comparing inferior epigastric artery (IEA) to other surgical Anastomosis techniques in renal allografts with MRA.

Methodology: The database MEDLINE was searched via PubMed, EMBASE, The Cochrane Library. Grey literature search was utilised including GoogleScholar. We appraised the studies using Keywords and MeSH were utilised, including: “epigastric artery” AND “kidney transplant”. The studies were appraised using Newcastle-Ottawa scale and meta-analysed using random-effects model.

Results: A total of eight studies met the inclusion and exclusion criteria for analysis. Five studies were included in the quantitative analysis. Majority of the studies were poor (n=4) or fair (n=4). There were a total of n=846 patients in the studies, with n=161(19.0%) undergoing inferior epigastric artery anastomosis. Other anastomosis techniques consisted of: side-to-side with single anastomosis, long or modified carrell patch, end to side to main renal artery with single anastomosis. Nearly all of the renal allografts in the study population consisted of living donation kidney allografts. In meta-analysis: there was no statistical difference in urological complication rate between IEA versus other techniques, O.R. 0.82 (CI 0.21, 3.24). There was a trend towards lower delayed graft function (DGF) in IEA versus other anastomosis techniques but it did not reach statistical significance (O.R. 0.45, CI 0.10, 2.02). In qualitative analysis, vascular complications were largely reported in one paper, with 3 in IEA vs 6 in other anastomosis group. Long-term graft function was only reported in one paper, with 2 (9.5%) in IEA vs 47(16.2%) in other anastomosis group. Overall follow-up ranged from 12 months to 10 years, with none reporting long-term patient survival.

Conclusion: Utilisation of recipient inferior epigastric artery for accessory polar vessels is an acceptable technique in renal transplantation. Whilst no short-term differences were shown in peri-procedural vascular or urological complication, there was a trend towards reduced delayed graft function. Long-term impact on graft function remains to be determined.
Pediatric Liver Transplantation Indications and Outcomes in Glycogen Storage Disease: A Single Center Experience

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1Department of Pediatric Gastroenterology, Baskent University, Ankara, Turkey; 2Department of Pediatrics, Baskent University, Ankara, Turkey; 3Department of Pediatric Metabolic Diseases, Baskent University, Ankara, Turkey; 4Department of General Surgery, Division of Transplantation, Baskent University, Ankara, Turkey.

Introduction: Glycogen storage diseases (GSDs) are inherited metabolic disorders result from impaired glycogen storage, glycogen or glucose breakdown. Liver transplantation (LT) is considered as a treatment option for patients with glycogen storage diseases present with hepatic malignancy, liver failure or metabolic decompensation. GSD type Ia is associated with mutations in the G6PC gene due to deficiency of glucose-6-phosphotase, while glycogen storage disease type 9 results from phosphofructokinase deficiency, an enzyme necessary for glycogen breakdown. Herein, we present our experience and transplantation outcomes in 7 pediatric patients with GSD who underwent LT.

Methods: We retrospectively analyzed data from patients diagnosed with GSD who underwent LT between 1993-2021 years.

Results: LT was performed in 6 patients with GSD type 1a and one patient with GSD type 9. Four patients had a family history of consanguinity (3 patients 1st degree, 1 patient 2nd degree). Mean age of diagnosis was 7.28 (1-24) months. Mean age of LT was 128.5 (13-216) months. Transplantation indications were hepatic adenoma (4/7), poor metabolic control (4/7) and cirrhosis (1/7). Extra-hepatic findings included proteinuria (4/7), Focal segmental glomerulosclerosis (1/7), proximal tubulopathy (4/7), nephrophtisisis (2/7), hyperlipidemia (7/7), delayed puberty (3/7), hypertension (2/7), short stature (6/7), epilepsy (2/7) and osteoporosis (4/7). One patient with GSD1a underwent cataract surgery. Three patients with GSD1a incidentally had the same G6PC gene mutations (c.247C>T). Three patients had normal cognitive functions and development (WISC-R Test). Two patients had mild where one patient had moderate mental retardation. One patient had %30 developmental delay (AGTE Test).

Six patients underwent LT from living-related donors while one patient had cadaveric donor. Patients who underwent LT from live donors received left lateral segment. Explant liver pathology revealed variable numbers (1-12) of hepatic adenoma in 4 patients. Hepatocellular carcinoma (HCC) was detected in one patient. Serum lactate, uric acid and triglyceride levels normalized after transplantation. In patients with DGF (34.5% vs 10.6%) p= 0.0001. In univariate analysis risk factors of DGF and different subgroups of kidney donors. It is associated with an increased risk of graft loss in adult KTX. Several factors related to donor, recipient, and organ procurement/transplantation procedures may increase the risk of DGF. The aim of our study was to evaluate the cumulative incidence of DGF in a children who received a kidney graft from a brain-dead donor, its impact on patient and graft survival, and to identify predictive risk factors of DGF.

Methods: A retrospective multicenter study was conducted including recipients under 18 years of age who underwent KTX from a brain-dead donor between January 1, 2015 and December 31, 2017. DGF was defined as the need for dialysis within the first week after KTX. Data were obtained from the clinical records of the patients and from the Registry and Management System of Argentina (SINTRA) and were analyzed using MedCalc® Statistical Software version 20.014; 2021.

Results: We analyzed 239 KTX performed at 17 centers. Of the recipients 54.4% were male, median age at Tx was 13.7 yr (r: 2.8 - 17.9), weight 30kg (r: 7 - 82), BMI 17 Kg/m2 (r: 11 - 36). Etiology of ESRD: CACUTX 30%, glomerular diseases with risk of recurrence 24.3%, typical HUS 3.8%, others 29.7%, and unknown 12.2%. Pre-emptive KTX was performed in 18.8% of patients, 59.7% were receiving hemodialysis, and 41.5% peritoneal dialysis. Median time of dialysis was 2.6 yr (r: 0.12 - 9.8). Of the donors 70.7% were male, median age was 17.6 yr (r: 2.8 - 55), BMI 23 Kg/m2 (r: 17 - 35), BMI ratio donor/recipient 1.35, and pre-ablation serum creatinine 0.82 mg/dl (r: 0.6 - 2.6). Cause of death was trauma in 57%, vascular in 24%, and others in 19%. Cold ischemia time was 16.6 hours (r: 4.2 - 42), HLA mismatches <= 3: 54% and <=4: 46%. Multiple-organ donor in 84.5%. Overall, 59 patients (24.7%) developed DGF. Patients without DGF had better graft survival at 1 (96% vs 78%) and 3 yrs of follow-up (89% vs 73%) p= 0.001. There were no significant differences in patient survival between both groups at the 3-year follow-up (95% vs 91%). Incidence of early AR (90 days post Tx) was higher in patients with DGF (34.5% vs 10.6%) p= 0.0001. In univariate analysis risk factors for DGF were: age at Tx > 13.7 yr, male gender, glomerular disease with risk of recurrence, hemodialysis as prior to KTX, and time on dialysis > 1 yr. In multivariate analysis independent risk factors for DGF were: time on dialysis > 1 yr (OR 9.2 - 95% CI 2.1 - 39) and age at KTX > 13.7 yr (OR 1.09 - 95% CI 1.01 - 1.18).

Conclusion: In our cohort, cumulative incidence of DGF was higher than that reported by other authors. Patients with DGF had worse graft survival than those without DGF. Shortening the time on dialysis seems to be a modifiable factor to reduce DGF.

Pediatric Kidney Transplantation in Argentina: Is Delayed Graft Function a Problem? Results of a Multicenter Study

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1Hospital de Pediatría “Juan P. Garrahan”, Buenos Aires, Argentina; 2GRUPO MIT, Santa Fe, Argentina; 3TáT Nephrology, Buenos Aires, Argentina; 4Hospital Privado Universitario, Cordoba, Argentina; 5Hospital Italiano, Buenos Aires, Argentina; 6Hospital Español, Mendoza, Argentina; 7Hospital de Alta Complejidad El Cruce, Buenos Aires, Argentina; 8Hospital Allende, Cordoba, Argentina; 9Hospital Almenar, Buenos Aires, Argentina; 10Hospital Universitario Austral, Buenos Aires, Argentina; 11Kidney Committee, SAT., Buenos Aires, Argentina; 12Technical and Scientific, INCUCAI, Buenos Aires, Argentina.

Introduction: Delayed graft function (DGF) is a manifestation of acute kidney injury occurring after kidney transplantation (KTX). Incidence of DGF in pediatric KTX recipients is variable (10% to 25%) due to different definitions of DGF and different subgroups of kidney donors. It is associated with an increased risk of graft loss in adult KTX. Several factors related to donor, recipient, and organ procurement/transplantation procedures may increase the risk of DGF. The aim of our study was to evaluate the cumulative incidence of DGF in a children who received a kidney graft from a brain-dead donor, its impact on patient and graft survival, and to identify predictive risk factors of DGF.

Methods: A retrospective multicenter study was conducted including recipients under 18 years of age who underwent KTX from a brain-dead donor between January 1, 2015 and December 31, 2017. DGF was defined as the need for dialysis within the first week after KTX. Data were obtained from the clinical records of the patients and from the Registry and Management System of Argentina (SINTRA) and were analyzed using MedCalc® Statistical Software version 20.014; 2021.

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Conclusion: In our cohort, cumulative incidence of DGF was higher than that reported by other authors. Patients with DGF had worse graft survival than those without DGF. Shortening the time on dialysis seems to be a modifiable factor to reduce DGF.
Immune Subset Differences by Flow Cytometry between Paediatric Kidney Transplant Recipients and Healthy Matching-age Paediatric and Adult Controls.

Elvira Jimenez Vera1, Haina Wang1, Patricia Anderson1, Catherine Lai2, Shounan Yi1, Wayne Hawthorne1, Natasha Rogers1, Peter Hsu2, Philip O’Connell1, Stephen Alexander3, Min Hu1.
1Centre for Transplant and Renal Research, Westmead Institute for Medical Research, Sydney, Australia; 2Allergy & Immunology lab, Children’s Hospital at Westmead, Sydney, Australia; 3Centre for Kidney Research, Children’s Hospital at Westmead, University of Sydney, Sydney, Australia.

Aim: Determine differences in immunophenotype of paediatric kidney transplant recipients vs. healthy matching-age paediatric and adult controls by minimum blood volume.

Methods: Absolute cell-count and leukocyte-profiling panels (46 fluorochrome-conjugated mouse-anti-human antibodies) for T cell, B, NK, DCs, and monocyte subsets were used to quantify immune-cell populations for 8 paediatric kidney transplant (PKTx) recipients, 5 healthy matching-age paediatric and 8 adult controls. Whole-blood sample (1050 µl) were used for flow-cytometry analysis.

Results: Absolute number of immune-cell subsets were in normal range for all groups. Age has correlation to CD45RO+memory T cells, but not to CD27+IgD-memory B cells. Healthy children had higher proportions of CD4-CD8-T (13.7±5.8 vs 7±4.3%, p=0.03) and γδT-cells (12±5.7 vs 5.4±4.6%, p=0.04), CD4+CD25+CD127-Tregs (10±1.4 vs 7±1.6%, p<0.01), lower proportion of HLA-DR+CD45RA-CD4+ (0.03±0.04 vs 7.4±5.6%, p=0.01), HLA-DR+CD45RA-CD8+ (0.0012±0.0018 vs 8±5.1%, p=0.04) T-cells compared to adults. HLA-DR was upregulated on both CD4+CD45RA- and CD8+CD45RA-T cells in PKTx, whilst CD183 (CXCR3) on CD4+CD45RO+ T-cells was downregulated. Compared to their healthy counterparts, PKTx had lower proportions of CD27+CD38lowclass-switch memory B-cells (38±7.6 vs 53±5.3%, p<0.01), non-classical monocytes (1.9±0.9 vs 5.8±1.1%, p<0.001), Tregs [CD4+CD25+CD127-Tregs (4.8±1.7% vs 10±1.4%, p<0.001) and CD4+FOXP3+Tregs (2.8±0.85% vs 6.3±1.3%, p<0.01)]. A small proportion of CD127+CD45RO+FOXP3 (2-5%) were observed in all groups. There was no difference in proportions of NK and DC between transplant vs control population.

Conclusion: Immune profiling by multi-colour flow cytometry revealed differences by ages and after transplantation and offers valuable insight into unique cell subset changes present in the transplant population that could be targeted clinically or to monitor patient condition.
Abstracts

**243.4**

**Evolution of Polyomavirus BK and JC Viral Load in Pediatric Renal Transplant Recipients**

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**Introduction:** Polyomavirus-associated nephropathy (PVAN) occurs in 5% of renal transplant recipients (RTR) and is caused by Polyomavirus BK (BKPyV) and JC (JCPyV), at a very low rate. This disease causes a progressive impairment of renal function and ultimate graft loss. Monitoring of viral load with pre-emptive reduction of immunosuppression is the only proved preventive strategy to reduce the risk of PVAN. The aim of this study was to describe the evolution of BKPyV and JCPyV viral load in de novo pediatric RTR.

**Method:** A prospective observational study was carried out in a pediatric RTR. Paired samples of serum and urine were collected at baseline (on the day of transplantation), then monthly for at least 9 months post transplantation (PostTx). Viral load of BKPyV and JCPyV was determined by a Multiplex Real Time PCR assay (transferred by Fedele CG, 2012).

**Results:** Fourteen patients were enrolled, the median age of the group was 13 years old (8-19) and 11 were male. The monitoring period was from 9 to 20 months (media 16). None of the patients developed PVAN during the study, but 11 (78%) of them tested positive, which were divided into three groups:

1. **BKPyV positive** (n=7) - they showed a pattern of viruria with a maximum between the 2nd and 7th month PostTx (median 8.5x10^8 copies/ml), after this peak viral load diminished significantly over the time getting undetectable in 4 cases. Two patients had higher values at the maximum in coincidence with impairment of renal function. Viremia was detectable in all cases, but with intermittences and it has not shown a well-defined profile, the highest values were around 10^4 copies/ml.

2. **JCPyV positive** (n=2) - both cases had JCPyV viruria without viremia with similar patterns: viral load was detectable from 2nd month PostTx and continued along the time with tendency to increase.

3. **BKPyV and JCPyV dual positive** (n=2) - BKPyV viruria and viremia were detected at low rates at the beginning, then appeared JCPyV viruria simultaneously but with higher viral load, and from 10th month PostTx to the end (17th month) only JCPyV viruria was detectable with the same upward trend as group two.

**Conclusion:** We detected active infection of BKPyV in 64% (9/14) of the cases, although there was no occurrence of any case of PVAN. However, in cases with impair renal function it were observed a significant increase of viruria. There are different proposed algorithms for monitoring BKPyV viral load to identify patients at risk of PVAN. We found a characteristic pattern of BKPyV viral shedding in urine. Based on this finding we would recommend to strengthen controls between 2nd to 7th month PostTx to be more sensitive to detect patients with viruria higher than 10^4 copies/ml, thus at more risk to develop viremia and consequently PVAN. Finally, when PVAN is suspected and BKPyV is undetectable, JCPyV diagnose should be made, since it can cause PVAN as well although with low frequency, and we demonstrated its presence in 29% of the cases.

Cesare Giovanni Fedele.

**243.5**

**Rabies Acquired Through Kidney Transplantation in a Child: A Case Report**

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Rabies is usually transmitted to humans through bites of infected animals; however, it can rarely be transmitted through deceased donor organs or tissues when not suspected. Here, we report a case of rabies transmission in a child. The child was a 5-year-old girl who was admitted to the pediatric intensive care unit with encephalitis of unexplained cause 3.5 months after she received a kidney transplant from a deceased donor. The laboratory and imaging studies did not reveal any explanation for her rapidly declining clinical and neurologic condition, which ended with death 4 days after admission. Death of another recipient from the same donor led to an investigation that revealed rabies as the cause. Both corneas were explanted from other recipients to prevent further death. Polymerase chain reaction sequence analysis of the corneas was consistent with a rabies virus from the same donor’s state of residence. Rabies transmission, although rare, should be suspected when a donor comes from or has visited endemic countries. Donors with unclear causes of death should be rejected.
243.6
PICU Length of Stay for Paediatric Liver Transplantation: A Single-Centre Experience From 2000-2021

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Introduction: With modern paediatric liver transplantation becoming increasingly resource-intensive, we endeavored to identify the factors that influence both PICU and Hospital length of stay (LOS) and evaluate the effect of a new customised anticoagulation protocol on LOS.

Methods: Data were obtained from the Liver Transplant and ICU databases for 336 transplants performed between 2000-2021 at the Children’s Hospital Westmead. Transplants were analyzed into two epochs, before and after June 2012, representing a change in post-operative anticoagulation management. Significant factors from a univariate regression analysis were included in a multivariate analysis. Significant factors were identified in the final regression models for both PICU and Hospital LOS. Missing variables were imputed using predictive mean matching.

Results: For PICU length of stay, a significant regression equation was found (F(8,301)=20.616, p<0.001), with an R2 of 0.360. Factors that predicted PICU LOS were: Time from Listing to Transplant (β=-0.139, p=0.004), Cold Ischaemic Time (β=0.104, p=0.041), Male Gender (β=0.088, p=0.064), Operation Time (β=0.108, p=0.024), CVVH (β=0.257, p<0.001), Delayed Abdominal Closure (β=0.323, p<0.001), Living Related Graft (β=0.090, p=0.077), and Graft vs. Recipient Weight Ratio (β=0.193, p<0.001).

For Hospital length of stay, a significant regression equation was found (F(6,286)=17.470, p<0.001), with an R2 of 0.275. Factors that predicted Hospital LOS were: PELD Score at Listing (β=0.136, p=0.010), Fluid Balance (β=0.124, p=0.020), CVVH (β=0.318, p<0.001), Cold Ischaemic Time (β=0.171, p=0.001), Whole Graft (β=0.077, p=0.064), and Biliary Atresia (β=0.216, p<0.001). There was a difference between Epoch one (Mdn=32.4 days) and Epoch two (Mdn=26.3 days) in Hospital LOS (U=9532, p<0.001), but not in PICU LOS (U=12756, p=0.969).

Conclusion: The introduction of the new anticoagulation protocol reduces Hospital LOS, but has no effect on PICU LOS. Patient, surgical, and management factors have been identified to PICU and Hospital LOS. These findings may provide impetus for considering changes in management and further research.

243.7
Survival After Surgical Management of Hepatoblastoma: Resection Versus Transplant

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Introduction: In children, hepatoblastoma (HB) is preferentially managed by hepatic resection (HR). However, in inestectable cases, liver transplantation (LT) is the only option. We compared outcomes following HR and LT for HB.

Methods: We retrospectively reviewed HB cases that underwent surgical management over a 25-year period (1996-2021). We assessed overall survival and disease-free survival at 1-, 5- and 10-years using the Kaplan-Meier method, log-rank tests, and multivariable Cox regression.

Results: We included 76 children, 46 (60.5%) male and 30 (39.5%) female, with a median age at diagnosis of 24.7 months (IQR: 9.41-50.38). HR was performed in 49 (64.5%) and LT in 27 (35.5%). Both groups were comparable by age, sex, alpha-fetoprotein levels, histology, and metastatic disease at diagnosis. The LT group had longer median time from diagnosis to surgery (4.4 vs 3.55 months; p<0.004), more multifocal tumors (51.9% vs 41%; p<0.001), and vascular invasion (63% vs 22.4%; p<0.001). Both groups had similar 1-, 5- and 10-year overall survival rates (p=0.97), respectively 93%, 89% and 87% for HR; and 100%, 93% and 85% for LT. Likewise, disease-free survival at 1, 5 and 10 years was 93.5%, 92.6% and 92.6% for HR; and 100%, 93% and 85% for LT (p=0.89). In multivariate analysis, metastatic disease at diagnosis (HR 6.14, CI 1.37-27.51), multifocality (HR 5.29, CI 1.49-18.74), and extrahepatic abdominal involvement (HR 11.11, CI 2.14-57.58) were associated with decreased overall survival.

Conclusion: Children with hepatoblastoma who underwent both HR and LT had excellent long-term overall survival. Multifocality, metastatic disease, and extrahepatic abdominal involvement impact outcomes.
Equality and Equity in Transplant for Children

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Introduction: Thomas E. Starzl, conducted the first paediatric liver transplant in 1963, a routine successful clinical procedure today due to his pioneering efforts. India, the second most populous country, 41% under 18 yrs of age, has followed on the heels of developed nations with 1522 pediatric transplants from 2013-2020 for all organs but majority done in private sector. To enable equality and equity, Govt of India has proposed establishing model transplant medicine in major government hospitals, at least one in each state in the latest National Organ Transplant Program Guidelines. Our aim is to develop an SOP for the establishment of paediatric transplant units in line with the Transplantation of Human Organs and Tissues Rules 2014, starting with VMMC & S.J.H.

Materials & Methods: In 2019, India reported 4,49,002 Road traffic accidents (RTA) with resultant 1,51,113 deaths. Delhi accounted for 5610 RTA with 1463 deaths. DD transplants prove to be exceptionally useful in diseases with high risk of recurrence particularly in children. VMMC & SJH is one of the largest govt tertiary care centres in Delhi catering to a large paediatric population and a large proportion of the RTA victims, the greatest source of deceased donor (DD) organs, if tapped. Living Donor Renal transplant is conducted in adult patients on a regular basis by urologists. A paediatric nephrologist being available, the paediatric renal transplant program can be started by a combined team of paediatric surgeons & urologists. Training in paediatric liver transplants can be done either locally in ILBS, Delhi or internationally through TTS-ILTS paired centers program similar to JIPMER, Pondicherry with St.James University hospital Leeds, UK. TTS in collaboration with NOTTO conducted an online survey of intensivists with regard to brain death declaration. The intensivists need to be trained for brain death declaration and donor maintenance to enable DD transplants. Augmentation of pediatric transplant intensive care beds and personnel is required along with round the clock lab facilities.

Results: The Govts of Delhi, Taminadu, Kerala, Maharashtra, etc have issued GOs for mandatory declaration of brain death in all patients who fulfill the criteria. DGHS has sought monthly submission of brain death data. Intensivist training for brain death declaration and donor maintenance was first started by NOTTO during the CAST 2019 congress and two more have followed. However, progress can only be achieved with implementation of training and establishment of dedicated centers.

Adherence Measurement in Adolescent Liver Transplant Recipients: Is It Useful for Long-term Outcome Assessment?

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Introduction: Advances in pediatric liver transplantation have led to an increasing number of patients reaching adolescence in whom poor adherence rate increases, becoming a prevalent risk factor for rejection and other adverse outcomes. Being a modifiable factor, its monitoring is a common practice in long-term follow-up and interventions on it are a priority for transplant programs. However, improvements in adherence do not correlate with long-term clinical results, these being the objective variables of graft functionality. The objective of this study is to correlate adherence measurement by both objective and subjective methods, with graft dysfunction and/or pathological liver biopsy, and to measure long-term clinical results as ideal transplant (single transplant, monodrug, no clinical complications associated with immunosuppression and normal growth).

Methods: Measurement and analysis of adherence using objective (variability in drug levels, >2 SD) and subjective methods (SMAQ questionnaire and medical impression) in 62 adolescents with liver transplantation who came for a follow up visit from August 2019 to March 2020 at Garrahan Hospital. Association was searched between the different adhesion methods and chronic graft injury (defined as three months or more of increased transaminases and/or pathological liver biopsy - rejection or fibrosis >2 on the Knodell-Ishak scale) using univariate logistic regression models. A p<0.05 was considered as significant, and STATA 15 was used.

Results: Of the patients surveyed, 50% were female, median age of 15.8 years (10.6-18.5), 10 patients received a retransplant (16%) and 40 had more than 10 years post-transplant (64.5%), 55.7% lived in CABA/AMBA and 40.9% in the rest of the country. No statistically significant association was seen between any of the adherence measurement methods with graft dysfunction and/or pathological liver biopsy (p 0.66 and 0.53 for variability, 0.96 and 0.11 for SMAQ questionnaire and 0.35 and 0.19 for subjective opinion). A total of 13 patients (21%) with ideal transplant results were obtained with a mean follow-up of 12.37 years.

Conclusion: With the data collected, it is not possible to correlate in a statistically significant way the measurement of poor adherence with graft dysfunction and/or pathological biopsies. Potential biases of this study are sample size, follow-up time and the population studied (adolescent group that attends control). However, since variability is an objective method and is related to adverse effects related to immunosuppression, we consider that drug measurement and its variability is the best method. Measurement of adherence is necessary since it allows evaluating interventions aimed at improving it, despite the fact that it is not directly related to clinical results. The focus on long-term transplant care has shifted to long-term consequences of immunosuppressive treatment, and it should be measured with objective variables (“ideal transplant”).
A Mixed-Method Systematic Review Examining the Effects of Digital Behaviour Change Interventions (DBCIs) Focussing on Improving Medication Adherence in Adolescent and Young Adult Kidney Transplant Patients

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Introduction: Non-adherence to immunosuppressants is one of the leading causes of premature transplant failure among adolescent and young adult kidney transplant recipients. An increasing number of studies have shown the effectiveness of DBCIs to promote treatment adherence in kidney transplant patients. The aim of this systematic review is to evaluate the effects of digital behaviour change interventions in young kidney transplant patients.

Methods: Searches were conducted through MEDLINE, PsycINFO, PubMed, CINAHL, Embase, Scopus, Google Scholar, and Web of Science to identify digital behaviour change interventions designed specifically for young kidney transplant patients. Potential studies were screened and selected independently by two researchers. Data were extracted and the risk of bias was assessed by one reviewer and validated by a second reviewer. The PRISMS taxonomy is used to describe the DBCIs.

Results: Initial searches resulted in a total of 901 studies with a final selection of 10 studies (8 quantitative, 2 qualitative). The overall quality of the studies was considered as moderate. 3 out of 10 studies included in this review comprised multi-component interventions to improve treatment adherence. Skills training, in conjunction with other forms of interventions, particularly phone counselling, was commonly employed and generally effective in improving self-management outcomes. The results of this review showed a positive correlation between the digital intervention and improved knowledge, social support and favourable clinical outcomes.

Discussion: Digital interventions such as mobile health applications, computer systems and multi-component interventions have the potential to improve treatment adherence in adolescents and young adult kidney transplant recipients. DBCIs can be used as a feasible tool for providing long-term, tailor-made interventions for young kidney transplant patients to improve the goals assessed.

Prediction of ESRD Risk in Living Kidney Donors Through Thirty Years Postdonation

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Introduction: Living kidney donors face increased risk of ESRD, although absolute risk remains low through 20 years postdonation. The ethical practice of living donor nephrectomy depends on accurate estimates of postdonation ESRD risk.

Methods: Using SRTR data 1987-2020, we modeled the association between donor characteristics and ESRD risk: age, sex, race (White/Black/Other), first-degree biological relationship to recipient, predonation systolic blood pressure, predonation eGFR, and BMI with multiple imputation to handle missingness. We censored for mortality and fit race-stratified models to investigate interactions.

Results: Among 158,304 donors, 589 experienced ESRD. Overall cumulative incidence of ESRD was 0.5% at 20 years postdonation, 1.1% at 25 years postdonation, and 1.5% at 30 years postdonation. 30-year risk of ESRD was higher for first-degree related donors (1.6% vs 0.9%), men (2.1% vs 0.9%), and Black donors (3.6% vs 1.1% White/1.5% Other) (all p<0.01). Older age was associated with increased ESRD risk among White donors but decreased risk among Black donors (Figure). Among nonwhite/nonblack donors, there was no monotonic relationship between age and ESRD risk, with the lowest risk for donors age 31-40 (0.95%) and highest for donors age>50 (2.1%). In multivariable models, higher SBP, BMI>30, and history of cigarette use were associated with increased ESRD risk. There was no evidence of association between predonation eGFR and postdonation ESRD risk, in unadjusted models or after adjusting for age, sex, race, and biological relationship to recipient. The final multivariable model predicted ESRD risk with C-statistic=0.71 (Table).

Conclusion: ESRD risk through 30 years postdonation varies substantially by donor characteristics, and can be estimated based on predonation characteristics. Donor candidates with high predicted risk should be counseled about their ESRD risk and postdonation behaviors that can preserve function in the remaining kidney.
244.2

18-Year Follow-up of Kidney Donation in the Living Donor Transplant Program at a Reference Pediatric Hospital

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Introduction: The frequency of living donor transplant has recently increased for several reasons. On one hand, due to the increased prevalence of advanced chronic kidney disease and the decrease in the number of suitable brain-dead donors, and on the other hand, due to the improvement in the safety of the procedure for the donor. Since the primary objective of living-donor kidney transplantation is to guarantee the safety of the donor, the scientific community has recently become interested in the possible long-term complications of kidney donation, since follow-up information on the health of donors is essential for understanding the risks and consequences of donation, support donation selection and provide informed consent. The objective of this study is to evaluate the evolution after nephrectomy of the living donor population in a reference pediatric hospital.

Methods: A cross-sectional study of the living donor’s outpatient database was carried out from October 2002 to December 2021. All donors who completed donation in this period of time were included. Surgical time, transoperative incidents, hospital stay, post-surgical complications and long-term behavior of creatinine clearance and proteinuria were analyzed.

Results: A total of 1332 patients who entered the living donor kidney transplant program were analyzed, 796 completed donation (59.75%) and 43 lost follow-up (5.4%). Of the remaining 753 donors, 409 were women (54.31%) and 344 men (45.68%). A total of 702 patients underwent left nephrectomy (93.22%), 50 right nephrectomy (6.64%), and one patient was suspended before completing surgery (0.13%). The median age at nephrectomy was 37.068 years (r=18-56 yrs). The mean surgical time was 128.77 minutes (r=25-170 min). Among transoperative incidents, 125 pleural and/or peritoneum openings (16.60%), 10 kidney decapsulations (1.32%), 9 tearings of different vessels (1.19%), 1 adrenal vessel avulsion (0.13%), and 1 ureteral injury (0.13%) were described. There was one case of cardiorespiratory arrest in the recovery area. The mean days of hospital stay were 2.64 days (r=1-32 days). Creatinine clearance and proteinuria levels were analyzed during a follow-up period of up to 18 years. 96 patients (12.74%) had a sustained decrease in creatinine clearance and proteinuria (>150 mg/d) was found in 16 patients (2.12%). There were 2 donor deaths, none of them related to renal failure.

Conclusions: Although some increases in urinary protein levels and decreases in creatinine clearance were described, none of our living donors developed kidney failure. Of the 2 reported deaths, one was attributed to colon cancer and the other to alcoholic pancreatitis consequences, none of them related to donation. We can conclude that nephrectomy for donation purposes is a safe procedure since we found no decrease in long-term survival or progressive renal dysfunction.

Abstracts

Table. Combined model of postdonation ESRD risk.

| Age 51+ | 1.52 2.14 2.93 | <0.001 |
| Race/ethnicity: | | |
| White | Reference |
| Nonwhite/nonblack | 1.13 1.46 1.89 | <0.01 |
| Black (18-30y) | 3.66 5.05 6.98 | <0.001 |
| Black (31-40y) | 2.50 4.75 6.44 | <0.001 |
| Black (41-50y) | 1.32 2.04 3.20 | <0.01 |
| Black (51+) | 0.71 1.37 2.63 | 0.37 |
| 1st-degree bio related | 1.43 1.86 2.43 | <0.001 |
| SBP <120 | Reference |
| SBP 120-129 | 0.92 1.32 1.88 | 0.133 |
| SBP 130-139 | 0.996 1.48 2.21 | 0.052 |
| SBP 140+ | 1.14 1.89 3.15 | 0.01 |
| BMI <25 | Reference |
| BMI 25-29 | 1.10 1.49 2.02 | 0.01 |
| BMI 30-34 | 1.67 2.42 3.51 | <0.001 |
| BMI 35+ | 1.83 3.09 5.19 | <0.001 |
| History of cigarette use | 1.45 2.60 4.69 | <0.01 |

**Bold** denotes statistical significance
External Validation of the Toulouse-Rangueil Predictive Model to Estimate Donor Renal Function After Living Donor Nephrectomy

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Background: Living donor kidney transplantation (LDKT) is the best treatment for end-stage kidney disease (ESKD). Long term follow-up data of the donors are reassuring but some donors will develop chronic kidney disease (CKD) and, rarely, ESKD. Precise tools to define these risks are lacking. A predictive model to estimate the 1-year post-donation glomerular filtration rate (eGFR) and risk of CKD was developed from a Toulouse-Rangueil cohort in 2017[1] and has been shown to have good correlation to the observed 1-year post-donation eGFR[2, 3]. We aimed to externally validate this predictive tool in the a cohort of patients who underwent LDKT at our center.

Methods: Retrospective analysis of the 364 LKD at our center from 1998 to 2020. After exclusion of 33 donors, in whom eGFR at 1-year was missing, the remaining 333 donors were included in this study. Observed eGFR using CKD-EPI formula at 1-year post-donation was compared to the predicted eGFR using the formula developed in Toulouse-Rangueil: postoperative eGFR (CKD-EPI, mL/min/1.73m^2) = 31.71 ± (0.521 × preoperative eGFR) – (0.314 × age). The ability of this formula to predict the observed GFR was analyzed by Pearson correlation, agreement was evaluated by the Bland-Altman plot and discriminative ability to predict CKD3-5 by the area under the receiver operating characteristic (ROC) curve and by plotting calibration.

Results: Patients’ characteristics of the 333 LKD are shown in table 1. Mean donor age was 47.3±10.6 years-old and most were female (71%). A good correlation (Pearson r = 0.67; P < 0.001) and concordance (Bland-Altman plot with mean difference of observed-predicted eGFR = +2.33 mL/min/1.73m^2; 95% limits of agreement -21.41 to 26.47 mL/min/1.73m^2; P < 0.001) were seen between predicted and observed 1-year post-donation eGFR.

Area under ROC curve (AUC) showed a good discriminative ability of the formula in predicting observed CKD at 1-year post-donation (AUC = 0.83; 95% CI: 0.78-0.88; P<0.001), as shown in Figure 2, with optimal cutoff corresponding to a predicted eGFR of 65.25.7 mL/min/1.73 m^2 (5.25ml above the equality cutoff), for which the sensitivity and specificity to predict CKD were respectively 77% and 75%.

Calibration curve, shown in Figure 3, exhibited an excellent prediction with slope = 1.000 and CITL = 0.000.

Conclusions: The formula developed in Toulouse-Rangueil was successfully validated in our cohort, a different European population than previous described [2, 3]. We must, anyway, emphasize that the optimal value of predicted eGFR was around 5mL/min higher than the equality cutoff for CKD3-5 detection at 1-year, an outcome that was correctly predicted (both its presence or absence) in every 3 out of 4 donors. This model represents a simple and accurate tool that may be used to assist in the evaluation of potential donors, particularly in the setting of current increasing donor age.

Table 1. Patient’s characteristics of the 333 living donors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=333</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD</td>
<td>47.3±10.6</td>
</tr>
<tr>
<td>Sex F/M, n (%)</td>
<td>236 (71) ±97 (29)</td>
</tr>
<tr>
<td>BMI, mean±SD</td>
<td>25.5±3.4</td>
</tr>
<tr>
<td>Smoking habits, n (%)</td>
<td>51 (15)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>50 (15)</td>
</tr>
<tr>
<td>Pre-donation Scr, mean±SD</td>
<td>0.75±0.16</td>
</tr>
<tr>
<td>Pre-donation eGFR, mean±SD</td>
<td>100.3±14.7</td>
</tr>
<tr>
<td>1-y post donation Scr, mean±SD</td>
<td>1050±22</td>
</tr>
<tr>
<td>1-y post donation eGFR, mean±SD</td>
<td>71.4±63.2</td>
</tr>
<tr>
<td>Predicted 1-y post donation eGFR, mean±SD</td>
<td>69.1±10.0</td>
</tr>
</tbody>
</table>

A. Discriminative ability to predict CKD (defined as eGFR <60 mL/min/1.73m^2)

<table>
<thead>
<tr>
<th>Observed eGFR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>65</td>
</tr>
<tr>
<td>≥60</td>
<td>160</td>
</tr>
</tbody>
</table>

McNemar’s exact test P=0.001, Sensitivity 77%, Specificity 75%, PPV 52%, NPV 90% 90%

<table>
<thead>
<tr>
<th>Predicted eGFR</th>
<th>&lt;60</th>
<th>≥60</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65.25</td>
<td>40</td>
<td>17</td>
</tr>
<tr>
<td>≥65.25</td>
<td>45</td>
<td>23</td>
</tr>
</tbody>
</table>

McNemar’s exact test P=0.001, Sensitivity 47%, Specificity 93%, PPV 70%, NPV 84%
Performance of Updated Estimated Glomerular Filtration Rate Equations in Black Living Kidney Donor Candidates

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Purpose: New estimated glomerular filtration rate (eGFR) equations using serum creatinine (Cr) and/or cystatin C (CysC) have been derived to eliminate adjustment by perceived Black ancestry. We sought to analyze the performance of newer eGFR equations in Black living kidney donor (LD) candidates.

Methods: Black LD candidates (n=64) who had measured iothalamate (i) GFR between 1/2015 and 10/2021 were included, and eGFR was calculated using race adjusted (Cr2009, Cr-CysC2012) and race unadjusted (Cr2021, Cr-CysC2021) CKD-EPI equations. Bias (eGFR-iGFR) and accuracy (percent within 30% of iGFR) were calculated.

Results: Mean age at LD evaluation was 41±12 yrs, and 45% were male. Mean iGFR was 105±23 ml/min/1.73m². Results are shown in Table 1. CKD-EPICr2021 eGFR showed a greater negative bias, and underestimated iGFR to a level < 80 ml/min/1.73m² in 11% with iGFR ≥ 80. Alternatively, the CKD-EPICr-CysC2021 equation showed less bias and high accuracy in the absence of correction for Black ancestry. In donor candidates with iGFR ≥ 80 ml/min/1.73m², none were estimated below 80 by the CKD-EPICr-CysC2021 equation. Eighteen Black candidates went on to donate and had eGFR measured at 6-18 months post-donation. By the Cr2021 equation, substantially more donors had an eGFR < 60 ml/min/1.73m² (44%), Table 2.

Conclusions: The CKD-EPICr/C2021 equation appears to underestimate true GFR in Black LD candidates, with the potential to exclude some for falsely low eGFR, and the potential to underestimate GFR post-donation. Alternatively, the recently recalibrated CKD-EPICr-CysC2021 equation appears to perform well in Black LD candidates, without negative bias or underestimation.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>CKD-EPI Cr2009</th>
<th>CKD-EPI Cr-CysC2012</th>
<th>CKD-EPI Cr2021</th>
<th>CKD-EPI Cr-CysC2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±SD (ml/min/1.73m²)</td>
<td>105±23</td>
<td>106±20</td>
<td>96±17</td>
<td>107±15</td>
</tr>
<tr>
<td>Bias (median, [P25,P75]) (ml/min/1.73m²)</td>
<td>-2.4 [-12.5,12.5]</td>
<td>8.0 [-6.8,10.9]</td>
<td>9.6 [-22.8,-6.2]</td>
<td>5.0 [-10.8,13.4]</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>79.7</td>
<td>89.1</td>
<td>85.9</td>
<td>89.1</td>
</tr>
<tr>
<td>% GFR &lt; 80 ml/min/1.73m²</td>
<td>10.9</td>
<td>7.0</td>
<td>4.7</td>
<td>18.8</td>
</tr>
<tr>
<td>% GFR &lt; 60 ml/min/1.73m²</td>
<td>10.9</td>
<td>7.0</td>
<td>4.7</td>
<td>18.8</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>CKD-EPI Cr2009</th>
<th>CKD-EPI Cr-CysC2012</th>
<th>CKD-EPI Cr2021</th>
<th>CKD-EPI Cr-CysC2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (P25,P75) (ml/min/1.73m²)</td>
<td>68.0 (64.3,78.9)</td>
<td>76.7 (70.4,83.1)</td>
<td>69.9 (67.8,79.9)</td>
<td>74.9 (69.9,81.4)</td>
</tr>
<tr>
<td>GFR &lt; 60 ml/min/1.73m² (%)</td>
<td>17.6</td>
<td>6.44</td>
<td>11.1</td>
<td></td>
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</tbody>
</table>
244.5

Reasons to Decline Potential Living Kidney Donors and Trends Over Time

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Background: Because of the increasing waiting time for kidney transplantation, transplant centers may feel pressured to liberalize living kidney donor selection criteria, as long as donor safety can be guaranteed. In this study, we report the most common reasons for declining potential living kidney donors. Furthermore, we compared characteristics of declined donors to accepted donors and investigated whether these changed over time.

Methods: We performed a single-center cohort study in 1412 potential living kidney donors who were evaluated for donation between 1982 and 2018. Of these potential donors, 173 (12%) were declined. Reasons to decline donation were retrieved from the decision letter in the electronic patient record. We collected and compared demographic characteristics (age, sex, estimated glomerular filtration rate (eGFR), weight, length, blood pressure) of declined and accepted donors. Trends over time in our center were assessed using univariable linear regression analysis in both declined and accepted donors.

Results: Most common reasons to decline a donor were renal artery calcification (and accompanying stenosis) (N=41, 24%), low eGFR (N=40, 23%), obesity (N=19, 11%) and suspicion of a malignancy (N=13, 8%). Mean±SD age was 60±11 years in the declined donors vs. 52±10 years in the accepted donors (P<0.001). Sex did not differ significantly between the groups (58% female in the declined vs. 54% in the accepted group, P=0.39). Estimated GFR was significantly lower in the declined group than the accepted group (81±14 mL/min/1.73m² vs. 91±13 mL/min/1.73m² respectively, P=0.001). Systolic blood pressure was significantly higher in the declined group, compared to the accepted group (131±14 mmHg vs. 128±14 mmHg respectively, P=0.02). In the declined group, 27% individuals used antihypertensive medication vs. 14% in the accepted group (P=0.001). Over time, eGFR became lower in the declined donors and BMI increased (St.β=−0.18, P=0.02 and St.β=−0.16, P=0.04 respectively), while these variables did not change in the accepted donors.

Conclusions: We show that in our center, renal artery calcification and low pre-donation eGFR are the most common reasons to decline potential living kidney donors. Declined donors were older, had higher blood pressure and lower eGFR, compared to accepted donors, and these differences increased over time. These findings inform the evaluation of living donor selection criteria. Better understanding of the long-term course and impact of renal artery calcification is needed to conclude on the validity of this reason.

244.6

Postoperative Health Status and Quality of Life After Pure Laparoscopic Donor Hepatectomy for Living Donor Liver Transplantation

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Background: Laparoscopic donor hepatectomy (LDH) for living donor liver transplantation has been performed in several specialized institutes. Surgical outcomes of LDH have shown comparable results to open donor hepatectomy (ODH), but the quality of life (QOL) after LDH is not known. This prospective questionnaire-based study was performed to assess health status and QOL of live liver donors before and after donor hepatectomy (DH).

Material and Methods: From May 2017 to February 2020, 70 liver donors who underwent donor hepatectomy (DH) were enrolled, and questionnaire items such as Enhanced Recovery after Surgery (ERAS) mobility scale (EMS), Body Image Questionnaire (BIQ), and EQ-5D-3L were examined up to one year after DH to evaluate postoperative recovery, body image satisfaction, and health status, respectively. During the study period, 45 LDH donors and two ODH donors were finally fully evaluated (Figure 1).

Results: Two patients in the ODH group were discharged on POD 8 and POD 10, respectively, with neither of the two achieving the level of being independently mobile (EMS ≥8). On the contrary, patients in the LDH group were considered independently mobile from POD 5 based on the mean EMS of 45 patients. The LDH group had a significantly higher mean EMS than the ODH group on POD 5 and 7 (P = 0.011, and P = 0.004, respectively, Figure 2). Body image score of the LDH group was significantly higher than that of the ODH group at one month after DH (17.8 vs. 15.0, P = 0.017). EQ-5D-3L index value and EQ-5D-3L VAS were not different from preoperative values at six months (P = 0.059) and one month (P = 0.217), respectively (Figure 3).

Conclusions: Donors undergoing LDH showed faster (within a month) mobility recovery and body image satisfaction to the level of preoperative status than donors undergoing ODH. In the evaluation of QOL using EQ-5D, donors who underwent LDH recovered to preoperative health status within six months, in accordance with previous studies of donors with ODH. A multicentre prospective study will be needed to compare the LDH and ODH groups.
Diaphragmatic Hernia Following Living Donor Hepatectomy: A Systematic Review of a Rare and Serious Complication

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Background: Living donor hepatectomy (LDH) is a complex and complicated surgical procedure with reported morbidity of 10 - 41%. Although, the majority of these complications fall under Clavien Dindo grade I/II. Diaphragmatic hernia (DH) is one of the life-threatening and under-reported complications observed following LDH. The aim of this study is to determine the incidence of DH following LDH and identify implicating causative factors through a review of literature.

Methods: Following PROSPERO registration, a systematic database search was conducted for published literature between 2000 to 2022 on Jan 5th 2022. Seventeen studies with 37 cases were identified and included in this literature review (Fig 1).

Results: Based upon the available data from the included studies and 7082 subjects who underwent LDH. Median patient age was 43 years (range 23-54) and most of the cases presented following right lobe hepatectomy 94.6% (35/37) within a period of <3 years. Incarceration of hollow viscera through diaphragmatic defect was presenting intraoperative feature in 62.5% donors, of which resection of bowel was required in 53.3% (Fig 2). Further, all patients had an uneventful postoperative recovery and were discharged in a satisfactory state with no reported recurrence in the literature.

Conclusions: The development of a DH following LDH should be considered a serious and life-threatening complication, which when recognized, requires immediate operative repair, as it is associated with a significantly higher risk of strangulation and incarceration of bowel segments.
Update on the Long-term Follow-up of Kidney Donors From A Single Center in Argentina (Hospital Italiano de Buenos Aires)

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1Nephrology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Introduction: Living kidney donors are selected upon kidney and overall health. Only those with a low/minimal risk of developing progressive CKD are accepted. Clinical studies have shown that the risk of developing end-stage renal disease (ESRD) in donors is similar to that in the general population Nonetheless, long-term follow-up is of utmost importance to ensure they are properly monitored and receive timely and adequate medical care. We present our updated data on the long term follow-up of our population over the last 22 years.

Methods: Our data includes laboratory and clinical data on 197 patients who were donors between 2000-2022. The variables analyzed were: 1) GFR as Scr, eGFR (CKD-EPI 2009) and 24-h CrCl. 2) Proteinuria as 24-h microalbuminuria. 3) Hypertension. 4) Body Mass Index. 5) Renal Functional Reserve (RFR). We correlated post-donation GFR with expected GFR (adjusted to age and single kidney). Pre-donation RFR was correlated with post-donation GFR. Univariate analysis was used to compare pre and post-donation variables.

Results: Pre-donation demographic and clinical/lab data are shown in Table 1. As expected, GFR was significantly lower after donation (table 2). Post-donation GFR was significantly lower from expected GFR (80.55 vs 88.64 ml/min/1.73 m², p < 0.0001). However, the CKD stage (KDIGO 2) was not different in either scenario (measured vs expected). 2 donors (1%) with microalbuminuria slightly higher than 27 mg/d were accepted for donation. After donation, the mean value for microalbuminuria was not different from pre-donation (p=0.22), and only 2 previously normoalbuminuric patients increased microalbuminuria above 27mg/d. Pre-donation hypertensives amount to 10.2% of our population. Out of the 177 normotensive donors, only 17 developed hypertension after donation (9.6%). Donors with a RFR > 45 % (median of our population) had a tendency towards a higher GFR assessed by 24h-CrCl (72.94 ± 16.89 vs 66.96 ± 17.31 ml/min/1.73 m², p = 0.119). BMI was not significantly different after donation (27.5 ± 8.2 vs 26.84 ± 5.3 kg/m², p = 0.35).

Conclusion: In our population, renal outcome was similar to that of healthy individuals after uninephrectomy. GFR was slightly lower than expected after uninephrectomy. However, it is unclear whether this difference is clinically significant.

Table 1

<table>
<thead>
<tr>
<th>Variable ( n= 197 donors)</th>
<th>Mean (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Female/Male)</td>
<td>53.8% / 46.2%</td>
</tr>
<tr>
<td>Age (years)</td>
<td>49.8 ( range 25-74)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.5 ± 8.2</td>
</tr>
<tr>
<td>eScr (mg/dl)</td>
<td>0.85 ± 0.18</td>
</tr>
<tr>
<td>eGFR (ml/min/1.73 m²) (CKD-EPI 2009)</td>
<td>93.72 ± 17.8</td>
</tr>
<tr>
<td>Follow-up (months)</td>
<td>66.17 ± 50.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10.2 %</td>
</tr>
<tr>
<td>24-h Microalbuminuria (mg/d)</td>
<td>27.5 ± 8.2</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-donation Mean (± SD)</th>
<th>Post-donation Mean (± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scr (mg/dl)</td>
<td>0.85 ± 0.18</td>
<td>1.13 ± 0.24</td>
</tr>
<tr>
<td>24-hCrCl (ml/min/1.73 m²)</td>
<td>106.58 ± 24.34</td>
<td>80.55 ± 20.08</td>
</tr>
<tr>
<td>CKD-EPI 2009 (ml/min/1.73 m²)</td>
<td>93.72 ± 17.8</td>
<td>69.38 ± 16.91</td>
</tr>
</tbody>
</table>
Robotic Versus Open Mini-Incision Living Donor Nephrectomy: Single Center Experience

Chandra Bhati1, SeungLee2, Amit Sharma2, Aamir Khan2, Dhiren Kumar2, Gaurav Gupta2, Marlon Levy2.
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Background: A minimally invasive approach is gold standard for living donor nephrectomy (LDN). Traditionally robotic surgery is commonly used for native nephrectomies and urological procedures, robotic LDN is being performed at very few centers worldwide. The robotic platform allows three-dimensional imaging of the surgical site and precise replication of human hand movements scaled down. Robotic surgery is associated with less tissue manipulation and earlier recovery with minimal incision. The aim of this study is to compare the short-term clinical outcomes between robotic-assisted donor nephrectomy (RDN) and open mini-incision donor nephrectomy (ODN) at a single center.

Methods: From 2016 to 2019, 141 consecutive cases involving RDN were analyzed at our single center. Patient outcomes were compared with those from a historical cohort of 191 patients who underwent ODN (7.9-cm incision) from 2010 to 2015. Medical records, including demographics, operation factors, perioperative outcomes, and complications were reviewed retrospectively.

Results: The RDN and ODN groups had a mean age of 42.8 and 41.4 years old, respectively (p = 0.31) as well as a mean BMI of 27.1 and 27.2, respectively (p = 0.76). Left-sided donor nephrectomy was performed in 102 patients (72.3%) via robotic approach and 88 patients (44.7%) via open approach (p < 0.001). Operative time was similar between both groups (194.0 for RDN vs. 197.8 min for ODN, respectively; p = 0.40). The RDN group presented with less blood loss than the ODN group (37.5 vs. 79.3 ml; p = 0.023). There was no open conversion case in the RDN group. Postoperative creatinine retention (1 for RDN vs 3 cases for ODN, p = 0.643), lymphatic leak (1 for RDN vs. 0 case for ODN, p = 0.417). The overall rate of complications was low and there was no statistically significant difference between the groups. Complications included stump bleeding (3 for RDN vs 1 case for ODN, p = 0.313), urinary retention (1 for RDN vs 3 cases for ODN, p = 0.064), and delayed recovery (1 for RDN vs. 0 case for ODN, p = 0.417).

Conclusions: RDN is a safe and minimally invasive technique with excellent clinical outcomes for living donors. The robotic approach has benefits over the traditional open approach, including shorter length of hospital stay and reduced intraoperative blood loss.

Health System Barriers and Facilitators to Living Donor Kidney Transplantation: A Tale of Two States With the Highest and Lowest Rates

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Purpose: Current efforts to increase living donor kidney transplantation (LDKT) entails identifying patient-level barriers and little is known about barriers that exist at the level of the health systems. The provision of transplantation in Canada is at the provincial level and there is wide variability in LDKT performance across different provinces. We aimed to learn and compare health systems with the best and the worst performance in LDKT, and to identify health system-level barriers to LDKT.

Methods: This study took the form of a comparative case study analysis. Case study research is an in-depth and non-interventional examination of a single case over time using retrospective and contemporary data. Data collection entailed semi-structured interviews, document review, and participant observation. Data were analyzed thematically to generate themes surrounding the attributes and processes of a health system that facilitate the delivery of LDKT to patients, and those that create barriers.

Results: In the best-performing province of Canada, five themes emerged as facilitators to the delivery of LDKT to patients. The relationship between two provincial organizations (a regional transplant and a regional nephrology order) was identified as key to enabling the mandate and processes for LDKT. On the other hand, in the worst-performing province, similar themes emerged as barriers to LDKT. Barriers were identified at the levels of organizational coordination, professional knowledge, resources, geography, and governance. Particularly, inconsistent coordination between regional clinics and transplant centers and poor role definition was seen to hinder and delay care processes.

Conclusion: By comparing two health systems with variable rates of LDKT, we have identified several real-world health system-level barriers to the delivery of LDKT to patients. Many of these barriers are modifiable and have implications for practitioners, policymakers, administrators, and patients.

This work is supported by a Gift of Life Institute Clinical Faculty Development Research Grant from the American Society of Transplantation and a Health Research Grant, Kidney Foundation of Canada.
Technical Aspects and Outcomes in Hepatic Venous Reconstruction of Left Lateral Segments With Special Emphasis on Anomalous Hepatic Vein in Pediatric Living Donor Liver Transplantation

Eduardo Fonseca1, Joao J Seda Neto1, Flavia F Feier2, Marcel M Benavides1, Rodrigo R Vincenzi1, Karina K Roda1, Caio Vieira1, Carolina C Magalhaes1, Paulo P Chapchap1.

HVOO was observed in this cohort study. The comparative analysis of the LLS graft Types, in the post-transplant outcomes. Up to last follow up no higher GVH/RVH correlation. It was observed a higher CIT average in the IIIb: 7 (2.31%). Comparative analysis of recipient and intraoperative variables

Background & Aims: One of the challenges in Segmental Liver Transplantation is the reconstruction of Hepatic Vein (HV). The occurrence of Hepatic Vein Outflow Obstruction (HVOO) can result in graft loss. The aim of this study was to describe the outcomes in different Types of HV distribution of Left Lateral Segments (LLS) grafts.

Patients & Methods: Children (< 18 years) who underwent a Living Donor Liver Transplantation (LDLT) with LLS grafts during the period from February 2017 to August 2021 with follow-up until February 2022. Retrospective cohort study through data review of medical records and from a prospectively collected data base. The LLS grafts were classified according to the number and distance between HV – Graft Hepatic Vein (GHV) classification, determining the vascular reconstruction performed. Type I: a single orifice; Type II: two close orifices – wedge unification; Type IIIa: two separated orifices up to 20 mm distance – venoplasty to achieve a single orifice and Type IIIb (Anomalous Hepatic Vein – AHV): two separated orifices beyond 20 mm distance – Homolog Vein Graft (HVG) interposition. Recipient and Intraoperative variables included age, diagnosis, recipient weight, PELD scores, ascites, Graft-to-Recipient Weight Ratio (GRWR), Graft Hepatic Vein (GHV) diameter, Recipient Hepatic Vein (RHV) diameter, GHV and RHV correlation, Cold Ischemia Time (CIT), Warm Ischemia Time (WIT), need for IVC exclusion during implant, use of PV graft and mesh closure. Post-LT outcomes included the occurrence of HVOO, early (> 30 days) portal vein thrombosis (EPVT), late (> 30 days) portal vein thrombosis (LPVT), hepatic artery thrombosis (HAT), and retransplantation.

Results: 303 LDLT were performed in which LLS grafts were used. According to the GHV classification, the distribution of the LLS grafts was Type I: 174 (57.42%), Type II: 97 (32.01%), Type IIIa: 25 (8.26%) and Type IIIb: 7 (2.31%). Comparative analysis of recipient and intraoperative variables showed Type IIIb grafts presented a higher proportion of larger LLS and consequently a higher GRWR, as well as a higher mean of GHV, consequently higher GHV/RHV correlation. It was observed a higher CIT average in the LLS that required vascular reconstruction in the bench surgery – Types IIIa and IIIb grafts. There was no statistically significant difference between the LLS graft Types, in the post-transplant outcomes. Up to last follow up no HVOO was observed in this cohort study. The comparative analysis of the cumulative graft survival rate showed no difference according to the LLS graft Type used.

Conclusion: The reconstruction of venous drainage plays as essential role in the surgical management of LDLT with LLS grafts. The use of HVG interposition is a good surgical strategy in the use of LLS grafts that have AHV.
may alleviate burden of tremor among SOTR and consequently contribute to improvements in HRQOL.

The TransplantLines Biobank and Cohort Study was financially supported by Astellas BV and Chiesi Pharmaceuticals BV. The funders had no role in the design of the study.

245.2 Evaluation of Methods to Obtain Peripheral Blood Mononuclear Cells From Deceased Donors Adjacent to Organ Procurement for Tolerance-Induction Protocols

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1Department of Transplantation Surgery, Karolinska University Hospital, Stockholm, Sweden; 2Centre for Apheresis and Stem Cell Laboratory, Karolinska University Hospital, Stockholm, Sweden.

Regulatory cell therapies have shown promise in tolerance-induction protocols in living donor organ transplantation. These protocols should be pursued in deceased-donor transplantation. Donor peripheral mononuclear cells (PBMCs) are an optimal source of donor antigens for the induction of donor-specific regulatory cells that are more effective than antigen non-specific regulatory cells. During the development of a regulatory cell tolerance induction protocol with organs from deceased donors, we compared three methods of obtaining PBMCs from deceased donors focusing on: cell yield, viability, and contamination of unwanted cell types.

PBMC procurement methods: During organ procurement at the time of cold perfusion, blood was collected from the vena cava and placed into a 10-liter blood collection bag, and thereafter transported to Karolinska University Hospital, where leukapheresis was performed (BCL) n=7. Blood was collected via the vena cava into blood donation bags before cold perfusion. The bags underwent buffy coat separation and thereafter automated leukocyte isolation using SEPA (BCS) n=2. To collect PBMCs, leukapheresis was performed via a central dialysis catheter on deceased donors in the ICU prior to the organ procurement procedure (LEU) n=9.

Our results show that all methods were safe in relation to the intended organ procurement procedure. LEU is a feasible method to obtain PBMC from deceased donors. LEU tend to have higher yield of donor PBMC/kg compared to BCS and BCL and acceptable level of granulocyte contamination compared to BCS.

Further investigations including the quality of the cell products that was manufactured with PBMCs from these methods will be needed to determine which approach is the most suitable for tolerance induction protocols.
Outcomes of Dialysis Dependent Second Kidney Transplant Recipients by Induction Type in the United States

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1Nephrology, University of Minnesota, Minneapolis, MN, United States; 2Complex Care Analytics, M Health Fairview, Minneapolis, MN, United States; 3Surgery, University of Minnesota, Minneapolis, MN, United States.

Background: We examined the association between induction type for second kidney transplant in dialysis dependent recipients and the long-term outcomes.

Material and Methods: Using the Scientific Registry of transplant Recipients SRTR standard analysis file, we identified all second kidney transplant recipients who returned to dialysis prior to re-transplantation. Exclusion criteria included: missing, unusual, or no-induction regimens, maintenance regimens other than tacrolimus and mycophenolate, and positive crossmatch status. We grouped recipients by induction type into three groups: Anti-thymocyte group (n=9899), Alemtuzumab group (n=1982) and IL-2 Receptor Antagonist group (n=1904). We analyzed recipient and death-censored graft survival (DCGS) using the Kaplan-Meier survival function with follow up censored at ten-year post-transplant. We used Cox proportional hazard models to examine the association between induction and the outcomes of interest. To account for center specific effect, we included center as a random effect. We adjusted the models for pertinent recipient and organ variables.

Results: In the Kaplan-Meier analyses, induction type did not alter recipient survival (log-rank p=0.419) or DCGS (log-rank p=0.146). Similarly, in the fully adjusted models, induction type was not a predictor of recipient or graft survival. Live-donor kidney was a favorable predictor of recipient survival [HR 0.73, 95% C.I. (0.65, 0.83), p<0.001] and graft survival [HR 0.75, 95% C.I. (0.66, 0.85), p<0.001]. Publicly insured recipients had worse recipient and allograft survival outcomes.

Conclusion: In this large cohort of second kidney transplant recipients, who were on dialysis prior to transplantation and discharged on tacrolimus and mycophenolate maintenance, induction type did not influence the outcomes of recipient or graft survival. Live-donor kidneys improved recipient and graft survival.
**Belatacept vs. Tacrolimus in the Real World: An Efficacy and Safety Analysis**

Karen Sofia K Gonzalez Arazo1, Jihan J Sleiman1, Gustavo G Laham1, Gervasio G Solar Pujo1, Carlos C Diaz1.
1Nefrología, Centro de educación médica e investigaciones clínicas, Buenos Aires, Argentina.

**Introduction:** Belatacept (B) is a co-stimulation inhibitor currently used as part of maintenance immunosuppression therapy in calcineurin-free regimens for renal transplantation (RT). Compared with Cyclosporine based regimens, B has shown no efficacy inferiority and less nephrotoxicity. We compared a de novo B (BG) based regimen vs. Tacrolimus (FKG) in a 5 year, ambispective observational study.

**Objective:** To compare a B based regimen vs. Tacrolimus in terms of efficacy and safety.

**Methods:** We included donor’s (D) and baseline recipient’s (R) demographic data. Follow data involved, creatinine, estimated glomerular filtration rate (eGFR), proteinuria (UP), acute rejection (AR), adverse events (AE), patient (PS) and death censored graft survival (DCGS). A D and R age and sex matched (1:1) sub analysis was performed between groups excluding living D RT. Differences were assessed using Student’s t-test, Mann-Whitney U-test, chi-square test, or Fisher’s exact tests, as appropriate. Survival curves were analyzed with Kaplan Meier.

**Results:** Before matching the study included 88 RT (BG: 25, FKG: 63). R on BG were older (63±11 vs. 52±12, p<0.001), received kidneys from deceased (92% vs. 68.3%, p 0.016) and older (54±16 vs. 51±13, p<0.001) D than FKG. Delayed graft function was higher in BG (76% vs. 27%, p<0.001). Pre transplant panel reactive antibodies, donor specific antibodies, number of re-transplants or use of polyclonal antibodies as induction therapy were not different between groups (Figure 1). After matching 23 R remained in each group. BG had significantly more extended criteria D (91.3% vs. 30.4%, p<0.0001) and a higher incidence of DGF (73.9% vs 30.4%; p<0.003). For the rest of the variables groups were comparables (Figure 2). During the first year of follow-up of the matched cohorts, BG showed higher creatinine values (1.65±0.58 vs. 1.33±0.39, p<0.036) and lower eGFR values (43.2±14 vs. 54.9±18, p<0.026). This difference disappeared with a trend towards reversal at the fifth year, creatinine values (1.17±0.25 vs. 1.55±0.59, p<0.122) and eGFR (50±16 vs. 40.7±12, p<0.122). There were no differences in the incidence of hypertension (HTN), malignancy, or infections between the groups (Figure 2). Patient survival was 90% and DCGS was 95% at one year with no differences between groups during follow-up.

**Conclusions:** In this study Belatacept showed comparable efficacy results with Tacrolimus with a trend towards a better renal function, similar patient survival and DCGS. Belatacept showed lower incidence of PTDM and higher incidence of CMV infection compared with Tacrolimus.
Efficacy and Safety of an Intensified Dosing Regimen of Enteric-Coated Mycophenolate Sodium in de Novo Kidney Transplant Recipients in China: A Prospective Cohort Study

Wenqing Xie1,2,3,4, Wenhan Peng1,2,3,4, Zhechi He1,2,3,4, Junhao Lv1,2,3,4, Wenhua Lei1,2,3,4, Rending Wang1,2,3,4, Hongfeng Huang1,2,3,4, Jianyong Wu1,2,3,4, Jianghua Chen1,2,3,4,
1Kidney Disease Center, the First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, People's Republic of China; 2Kidney Disease Immunology Laboratory, State Administration of Traditional Chinese Medicine of China, Hangzhou, People's Republic of China; 3Institute of Nephrology, Zhejiang University, Hangzhou, People's Republic of China; 4Key Laboratory of Kidney Disease Prevention and Control Technology, Zhejiang Province, Hangzhou, People's Republic of China.

Introduction: Previous study showed the standard dose of immunosuppressants enteric-coated mycophenolate sodium (EC-MPS) might result in unsatisfactory control rate of effective blood concentration and improvable acute rejection rate. This prospective cohort study was designed to evaluate the efficacy and safety of an intensified dosing regimen of EC-MPS in de novo kidney transplant recipients in China.

Methods: This prospective cohort study enrolled patients underwent de novo renal transplantation from 2015.6 to 2018.9. Participants were divided into the intensified-dose (week 1: 2160 mg/day; week 2: 1440 mg/day; followed by 720-1080 mg/day) and standard-dose (week 1: 1440 mg/day; week 2: 1080 mg/day; followed by 720-1080 mg/day) groups. Sub-group were analyzed based on mycophenolic acid (MPA)-area under the concentration (AUC): achieved group (defined as patients whose MPA AUC is equal or beyond 40 mg.h/L within Day 7) and under exposure group (defined as patients whose MPA AUC is below 40 mg.h/L within Day 7). The primary endpoints were 12-month-biopsy-proven acute rejection (BPAR), graft and patient survival rates. safety were also assessed. The study was followed up 3 years.

Results: A total of 128 patients were included, with 65 and 63 patients in the intensified-dose group and standard-dose group, respectively. The 12-month-BPAR incidence was numerically lower in the intensified-dose group than standard-dose group (4.6% vs. 9.5%, p=0.320). The rate of patients achieving target mycophenolic acid (MPA)-area under the concentration (AUC) achieved group (defined as patients whose MPA AUC is equal or beyond 40 mg.h/L within Day 7) and under exposure group (defined as patients whose MPA AUC is below 40 mg.h/L within Day 7). The primary endpoints were 12-month-biopsy-proven acute rejection (BPAR), graft and patient survival rates, safety were also assessed. The study was followed up 3 years.

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Conclusion: Intensified dosing of EC-MPS results in a numerically lower incidence of 12-month-BPAR and lower positive incidence of dnDSA with 36 months follow up. Intensified dosing could help achieve target therapeutic blood concentration of EC-MPS, that showed significantly lower BPAR and no more infection incidence increased and might further improve long-term prognosis in Chinese de novo kidney transplantation recipients.

Table 1 Outcomes

<table>
<thead>
<tr>
<th>Primary outcomes</th>
<th>Intensified-dose group (n=65)</th>
<th>Standard-dose group (n=63)</th>
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<tbody>
<tr>
<td>12-month-BPAR incidence (n, %)</td>
<td>6 (9.5)</td>
<td>6 (9.5)</td>
<td>0.500</td>
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<tr>
<td>12-month patient survival rate (n, %)</td>
<td>64 (98.5)</td>
<td>63 (98.5)</td>
<td>0.800</td>
</tr>
<tr>
<td>12-month graft survival rate (n, %)</td>
<td>64 (98.5)</td>
<td>63 (98.5)</td>
<td>0.800</td>
</tr>
</tbody>
</table>

Secondary outcomes

<table>
<thead>
<tr>
<th>AUC (mg.h/L)</th>
<th>Achieved group (n=59)</th>
<th>Under exposure group (n=63)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>12-month BPAR incidence (n, %)</td>
<td>6 (10.2)</td>
<td>6 (10.2)</td>
<td>0.990</td>
</tr>
<tr>
<td>12-month patient survival rate (n, %)</td>
<td>64 (98.4)</td>
<td>63 (98.4)</td>
<td>0.990</td>
</tr>
<tr>
<td>12-month graft survival rate (n, %)</td>
<td>64 (98.4)</td>
<td>63 (98.4)</td>
<td>0.990</td>
</tr>
</tbody>
</table>

Table 2 Comparison between the achieving and non-achieving target MPA-AUC groups

<table>
<thead>
<tr>
<th>Achieving target MPA-AUC group</th>
<th>MPA-AUC (mg.h/L)</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Achieving target MPA-AUC group</td>
<td>3-month BPAR incidence</td>
<td>3 (4.6)</td>
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<tr>
<td>Achieving target MPA-AUC group</td>
<td>3-month patient survival rate</td>
<td>100 (100.0)</td>
</tr>
<tr>
<td>Achieving target MPA-AUC group</td>
<td>3-month graft survival rate</td>
<td>100 (100.0)</td>
</tr>
<tr>
<td>Achieving target MPA-AUC group</td>
<td>3-month DGF incidence</td>
<td>8 (12.5)</td>
</tr>
<tr>
<td>Achieving target MPA-AUC group</td>
<td>3-month infection incidence</td>
<td>20 (20.0)</td>
</tr>
</tbody>
</table>

Data are presented as n (%). BPAR: biopsy-proven acute rejection; DGF: delayed graft function; MPA: mycophenolic acid; AUC: area under concentration.
Belatacept as Primary Immunosuppression in Patients With Cardiac Transplantation

Vanina V Barranco B1, Elisa E Corri C1, Sebastian S Jauretche J1, Marisol M Ferrer E1, Sebastian S Rodriguez R1, Maire M Escobar E1, Martin M Rodenas R1, Ivan I Bertolin B1, Alfredo A Buscemi B1, Ricardo R Pereyra P1, José Luis JL Sgrosso S1.

Introduction: Calcineurin inhibitors (CNIs) are nephrotoxic and have broad pharmacological interactions, which may be a problem in the treatment of transplant patients who use them. Belatacept is a non-nephrotoxic immunosuppressant whose function is the selective blockade of co-stimulation without demonstrated interaction with other drugs. Currently, scientific evidence supports the use of Belatacept in kidney transplants, however, in heart transplant recipients there is still not enough evidence for its indication.

Objectives: To present four patients with orthotopic cardiac transplantation (OCT) who received Belatacept as primary immunosuppression in CNI-free regimen, one of them for previous renal failure and three for neurological pathology.

Clinical Cases: A 72-year-old male with necrotic ischemic cardiomyopathy was transplanted in September 2014, with a glomerular filtration rate (GFR) of 45 ml/min (MDRD-4). A 63-year-old man with chagasic cardiomyopathy, who received an OCT in June 2015. He had seizures and previous stroke, and was being treated with phenytoin. A 51-year-old man with necrotic ischemic cardiomyopathy, who received an OCT in October 2018. With cardiac arrest recovered with transient cerebral ischemia and mild renal failure in post transplantation. A 61-year-old male with chagasic cardiomyopathy, who was transplanted in July 2021 with PRES Syndrome post transplant.

Because of these issues, the team decided to use Belatacept after obtaining informed consent. All received: Thymoglobulin 1.5 mg/kg/day for 5 days, 3 pulses of methylprednisolone, mycophenolate mofetil 2 g/day from day two and steroids were reduced as scheduled. Belatacept scheme: 10 mg/kg per pulse 1, 14, 28, 56 and 84 post transplant. From day 112 until now they have received Belatacept at a dose of 5 mg/kg every 28 days.

Conclusion: Tolerability to Belatacept was acceptable and patients did not develop acute episodes of graft rejection. Significant improvement in GFR and management of seizures was observed. However, clinical trials are insufficient to evaluate the efficacy and safety of Belatacept in patients with heart transplantation.

Is Incidence of Post-transplant Diabetes Mellitus Higher With Adoport Compared to Prograf in Patients Post Renal Transplantation?

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1Department of Renal Medicine, University Hospital. University Hospitals Coventry & Warwickshire NHS Trust, Coventry, United Kingdom.

Introduction: Post-Transplant Diabetes Mellitus (PTDM) refers to those diagnosed with diabetes mellitus after receiving a solid organ transplant. PTDM in the renal transplant patient has been associated with adverse cardiovascular disease outcomes, higher rates of graft rejection and infection. Current literature has reported the incidence of PTDM ranges from 9% to 39% within the first year post transplant. Commonly used immunosuppressants e.g. Tacrolimus can increase risk of PTDM. In recent years, many regional renal centres in the United Kingdom (UK) have changed Tacrolimus formulations from Prograf® (Brand) to Adoport® (Generic). This was mainly due to cost saving implications. At our local adult renal transplant centre in the UK, we have anecdotally speculated a higher incidence of PTDM between the two formulations. Thus, we have reviewed our incidence of PTDM in both groups.

Method: Data was obtained from our centre’s patient database on all adult patients who received a kidney transplant (living & deceased donor) between 2013 to 2019. Our criteria for diagnosing PTDM was in concordance with international recommendations. Incidence of PTDM was reviewed for the following cohorts: those patients on Prograf® only versus Adoport® only. Incidence was reviewed within 12 months, 12-24 months and 24 months post transplant. Fisher exact statistical analysis was used.

Results: Between 2013-2019, 452 patients received a renal transplant at our centre. 204 patients were started on Prograf®, 213 on Adoport®. The remainder were not on either medication. After further exclusion criteria, a total of 198 patients were identified with 24 months follow up post transplant (111 in Prograf® cohort, 87 in Adoport® cohort). At 12 months follow up post-transplant, the overall incidence of PTDM in both cohorts was 8.6% (17/198). Adoport® cohort (10/87) had a higher incidence of PTDM compared to Prograf® (7/111), [11.5% versus 6.3% p=0.21]. Between 12-24 months post transplant, two further patients on Adoport® developed PTDM compared to one further patient in Prograf® cohort. Cumulatively, over a 24 months period, our study showed an overall incidence of PTDM in both cohorts of 10.1% (20/198). Similarly, there was a higher incidence of PTDM in the Adoport® group (12/87) compared to Prograf® (8/111), (13.7% versus 7.2%, p=0.16). Average time to diagnosis of PTDM was 6.9 months (Prograf®) compared to 7.0 months (Adoport®).

Conclusion: At present, we are the only study in medical literature to compare different formulations of Tacrolimus (Adoport® and Prograf®) and their incidence of PTDM in renal transplant patients. Our data suggested a higher incidence of PTDM in those renal transplant patients who take Adoport® compared to Prograf®. Although our findings were not statistically significant, likely due to small sample size, further research into the different preparations of Tacrolimus’ risk of developing PTDM is warranted.
Effect of CYP3A5 Genotype-Guided Versus Conventional Initial Dose of Tacrolimus in Children With Kidney Transplants

Ana Catalina Alvarez-Elias¹, María del Pilar García-Roca¹, Luis Velasquez-Jones², Saul Valverde-Rosas², Gustavo Varela-Fascinetto³, Mara Medeiros-Domingo¹.

¹Unidad de Investigación y Diagnóstico en Nefrología y Metabolismo Mineral Oseo, Hospital Infantil de México Federico Gomez, Delegacion Cuautemoc, Mexico; ²Departamento de Nefrología, Hospital Infantil de Mexico Federico Gomez, Delegacion Cuautemoc, Mexico; ³Cirugía de Trasplante, Hospital Infantil de Mexico Federico Gomez, Delegacion Cuautemoc, Mexico.

Background: CYP3A5 tacrolimus polymorphisms predict its metabolism. We aimed to test the advantage of a genotype-guided starting dose after kidney transplantation to reduce the time to target drug levels and improve allograft surveillance.

Methods: We performed a single-center, open-label parallel group, randomised controlled trial in kidney recipients (0-18 y/o) at the Hospital Infantil de Mexico, Federico Gomez, from Jan-2013 to Dec-2018. Patients were assigned to one of two groups. The genotype-guided group received the dose according to the CYP3A5 polymorphisms (AA1*1, AG1*3 [expressers], and GG3*3, [non-expressers]). The Conventional-dose group received standard of care. We followed them for 12 months registering time to target levels, estimated glomerular filtration rate (eGFR), rejection, and nephrotoxic events.

Results: We included 81 patients; 40 received the genotype-guided dose, the mean age at transplantation was 13.3 y/o, 51.8% were female. There was a higher frequency of expressers in the genotype-guided than the conventional-dose group (29.6 Vs 16.1% p=0.04), having a higher number of AA1*1. There were no differences in the time to achieve levels within groups. The subgroup analysis by genotype showed that expressers in the genotype-guided dose group took longer to achieve target levels (mean 5 vs 3.2 weeks, log-rank= 0.383).

Conclusions: Tacrolimus CYP3A5 genotype-guided initial dose after kidney transplantation did not show benefits on time to target levels, rejection, tac related nephrotoxic events or eGFR after a 12-months follow-up in our cohort. The higher frequency of expressers in the genotype-guided group could influence the results, showing a high impact of the polymorphisms. New dosing strategies are needed to improve accuracy.
Abstracts

245.10

Very Low Dose Anti-thymocyte Globulins Versus Basiliximab in Non-immunized Kidney Transplant Recipients

Christophe Masset1,2, Clarisse Kerleau1, Gilles Blancho1,2, Maryvonne Hourmant1,2, Diego Cantarovich1, Aurélie Houzet1, Magali Giral1,2, Claire Garandeau1, Jacques Dantal1,2.

1Service de Néphrologie et Immunologie Clinique, Institut de Transplantation Urologie Néphrologie, Nantes, France; 2Center for Research in Transplantation and Translational Immunology, UMR 1064, Université de Nantes, Nantes, France.; DIVAT Nantes Consortium.

Background: The choice between Basiliximab (BSX) or Anti-Thymocyte Globulins (ATG) as induction therapy in non-immunized kidney transplant recipients remains uncertain. Whilst ATG can permit steroid withdrawal and CNI decrease, it also increases the risk of viral reactivations due to a prolonged dose-dependent lymphopenia. We compared transplant outcomes in non-immunized patients receiving a very low dosage of ATG (75 mg daily twice) versus BSX as induction therapy.

Methods: We included non-immunized patients receiving a first kidney transplant between 2015 and 2020. Studies outcomes were patient and graft survival, cumulative probabilities of acute rejection, infectious episode, CMV infection and Post-Transplant Diabetes (PTD). Cox, logistic or linear statistical models were used depending on the studied outcome and models were weighted on propensity scores.

Results: 183 patients were included, 100 receiving ATG and 83 receiving BSX. Maintenance therapy was comparable between groups. Patient and graft survival did not differ between groups, as infectious and CMV episodes. There was a trend to a lower occurrence of BPAR in the ATG group (HR at 1.92; 95% CI: 0.77; 4.78, p-value = 0.1598). Occurrence of PTD was significantly higher in the BSX group (HR at 2.44; 95% CI: 1.09; 5.46; p-value = 0.0304), due to a high number of treated rejection episodes (14.5% vs 7%).

Conclusion: Induction with a very low dose of ATG in non-immunized recipients is safe, decreasing the occurrence of treated rejections episodes compared to BSX, thus leading to a lower rate of PTD.
**245.12**

**4-Octyl Itaconate Inhibits T Cells' Proliferation and Aerobic Glycolysis to Prevent Immune Over Activation**

Yao Deng¹, Lujuan Chen¹, Lu Cao¹, Juan Zhang¹, Wei Wang¹, Xiaoqian Ma²

¹Cell Transplantation and Gene Therapy Institute, The Third Xiangya Hospital, Central South University, Changsha, People's Republic of China.

**Introduction:** Classically activated T cells require glycolysis for survival, differentiation, and effector functions, suggesting that targeted metabolism may be a therapeutic target in autoimmune diseases such as GVHD. T cells play an irreparable role in the occurrence and development of aGVHD. 4-OI has anti-inflammatory effects by targeting GAPDH to reduce aerobic glycolysis in macrophages. However, the effect of 4-OI on lymphocytes has not been shown. We hypothesized that 4-OI might target GAPDH downregulation aerobic glycolysis of lymphocytes and prevent immune over activation.

**Method:** Cells proliferation was detected by Ki67 and CFSE. The GAPDH activity assay kit was used to detect GAPDH activity. Cells metabolism were examined by Seahorse. The secretion of cytokines were detected by CBA and flow cytometry. We established an aGVHD model in mice. After 4 weeks, evaluated the severity of GVHD by clinical score and pathology score. BALB/c donor T cells expressing luciferase linked to the β-actin promoter and used BLI to measure the expansion of donor T cells.

**Results:** In vitro experiments, we did not find differences in survival rate of CD4/CD8 Tcells (92±2%) treated with different 4-OI concentrations. GAPDH activity in activated CD4/CD8 Tcells treated with 4-OI was considerably lower compared to activated cells. The proliferation of activated CD4/CD8 Tcells increased significantly, whereas 4-OI treatment greatly suppressed proliferation (CD4 60% vs 9%, CD8 78% vs 20%). 4-OI administration greatly lowered glycolysis capacity and MAX ECAR. It suggests that 4-OI can alter T cells' metabolic patterns. Finally, we discovered that activated cells generate cytokines. Cytokine production decreased considerably in activated CD4/CD8 Tcells treated with 4-OI compared to activated cells. CD4 Tcells (IFN-γ 14% vs 0.4%, TNF 16779pg/ml vs 12095pg/ml, CD107A 56% vs 24%, Granzyme B 26% vs 16%), CD8 Tcells (IFN-γ 13% vs 4%, TNF 2311pg/ml vs 880pg/ml, CD107A 53% vs 16%, Granzyme B 51% vs 28%). In GVHD disease model mice, 4-OI treatment reduced GVHD sign manifestations and clinical scores, and improved survival rates. BLI imaging showed that 4-OI treatment resulted in a significant decrease in proliferation of donor T cells. In the 4-OI treatment group, the glycolysis rate of Tcells from spleen of recipient mice was significantly decreased. And when we detected the cytokines of the serum, the levels of TNF-α, IFN-γ, IL-10, MCP-1, IL-12p70 and IL-6 from 4-OI treatment group were also greatly reduced compared to the control group.

**Conclusion:** In this study, we demonstrated that 4-OI did not affect the viability of rest T cells however it could inhibit the proliferation and function of activated T cells by decreasing aerobic glycolysis which suggested 4-OI a potential therapeutic agent in GVHD and autoimmune diseases.

*Natural Science Foundation of Hunan Province, China (Grant No.:2021JJ31018).*

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**245.13**

**CYP3A5 Polymorphism in Renal Transplantation: A Key To Personalized Medicine**

Prasad Gurjar², Amit Pasari¹,², Amol Bhawane², Priyanka Tolani³, Sanjay Kolte⁴, Vijay Katekhole¹, Manish Balwani¹,²

¹Department of Nephrology, Saraswati Kidney Care Center, Nagpur, India; ²Department of Nephrology, Jawaharlal Nehru Medical College, Wardha, India; ³Department of Medicine, Jawaharlal Nehru Medical College, Wardha, India; ⁴Department of Urology, Jawaharlal Nehru Medical College, Wardha, India; ⁵Department of Urology, Saraswati Kidney Care Center, Nagpur, India.

**Introduction:** Renal transplant (RTx) is the ultimate treatment option for end-stage renal disease (ESRD) patients. Tacrolimus (TAC) is an essential immunosuppressant drug for prevention of rejection in transplant patients. However, TAC has a narrow therapeutic window and its metabolism is affected by the genetic polymorphisms in CYP3A5 gene. TAC dose to maintain the required trough levels may differ according to type of gene polymorphism. In our practice, we observed CYP3A5*3 A6986G polymorphism (GG genotype) as being common finding in most patients undergoing transplant. This prompted us for routine evaluation of CYP3A5 polymorphism for all transplant patients preoperatively. Here, we present the distribution of CYP3A5 genetic polymorphism in evaluated patients and provide TAC dose in different types of polymorphism.

**Method:** In this retrospective, observational study, the electronic database of our center was screened to identify patients who have been evaluated for genetic polymorphism in CYP3A5 gene. In all patients, genetic analysis was carried via blood sample using polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) method. Data was analyzed descriptively. We considered trough TAC levels of 7 to 10 ng/ml within first six months and 3 to 7 ng/ml after six month of transplant as normal therapeutic levels.

**Results:** Between January 2017 and 10 March 2022, a total of 31 patients were identified, of which three had wild-type polymorphism. In the remaining 28 (90.0%) cases, CYP3A5*3 A6986G polymorphism was homozygous and heterozygous in 17 (60.7%) and 11 (39.3%), respectively. Among 28 cases, 14 (50.0%) had been diagnosed before transplant. In the 15 who have undergone transplant, 9 (60.0%) and 6 (40.0%) had homozygous and heterozygous polymorphism respectively. Of 15 cases, three did not receive TAC. Table 1 provides the details of dose of TAC required to achieve trough therapeutic levels in first six months and after six months of transplant stratified by type of polymorphism.

**Conclusion:** In our geographical area, CYP3A5*3 polymorphism is highly prevalent. We recommend genetic analysis to detect this polymorphism in all planned renal transplant patients. This strategy will help to reduce post-transplant TAC toxicity and will help in achieving personalized immunosuppression. We acknowledge Ms. Simran Bhanushali and Ms. Nikita Thakre for their contribution in data entry.

<table>
<thead>
<tr>
<th>Type of polymorphism</th>
<th>Mean TAC dose (mg/kg)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Within six months</td>
</tr>
<tr>
<td>Homozygous</td>
<td>0.044 (n=4)</td>
</tr>
<tr>
<td>Heterozygous</td>
<td>0.028 (n=2)</td>
</tr>
</tbody>
</table>

Numbers in parentheses represents available data.
Antibody Response and Cellular Phenotyping in Kidney Transplant Recipients Following SARS-CoV-2 Vaccination

Nicole Ali1, Zoe Stewart1, Jake Miles2, Sagna Mehta1, Vasishta Tatapudi1, Bonnie Lonze1, Elaina Weldon1, Charles Dimaggio1, S Gray-Gaillard1, Jeanette Leonard1, S Tuen1, Robert Montgomery1, Herati Ramin1.

1Transplant Institute, NYU Langone Health, New York, NY, United States; 2CareDx, CareDx, Brisbane, CA, United States.

Introduction: Correlates of protection for SARS-CoV-2 vaccines are not yet well-established in kidney transplant recipients (KTRs). Studies have highlighted the importance of neutralizing antibodies (Abs), however data suggests T cell responses may play a secondary role in preventing reinfection. We performed a longitudinal assessment of immunogenicity and T and B cell responses in KTRs following SARS-CoV-2 vaccination.

Methods: KTRs eligible for SARS-CoV-2 vaccination were screened through medical records from March 12, 2021. Baseline and weekly blood samples were collected for routine assessment, SARS-CoV-2 spike protein Abs titers and cellular phenotyping for 12 weeks. Ab response was defined as a 10-fold increase in total binding IgG titers. To determine if T cell responses were induced by vaccination, we considered the proportion of activated non-naive CD4+ and CD8+ T cells after vaccination.

Results: 49 KTRs with a mean age of 54 years were enrolled (Table 1). 10 patients (20.4%) mounted an Ab response following completed vaccination. A history of COVID-19 was associated with an increased likelihood of developing an Ab response (OR: 18.3, 95% CI 3.2, 105.0, p=0.0005). For non-naive CD8+ T cells, a subset co-expressing CD38+Ki67+ was induced 1 week after the 1st immunization in some SARS-CoV-2-naive patients (P=0.12 versus P=0.14 for SARS-CoV-2-experienced adults, Figure 1A/B). For non-naive CD4+ T cells, induction of a subset co-expressing CD38+Ki67+ was observed at 1 week after the 1st immunization for SARS-CoV-2-naïve participants (P = 0.09 for SARS-CoV-2-naive, P=0.03 for SARS-CoV-2-experienced adults, Figure 1C/D). For CD8+ and CD4+ T cells, dose 2 stimulated weak induction of the CD38+Ki67+ subset in the SARS-CoV-2-naive patients only (Figure 1A-D).

Conclusions: Quantitative Ab responses were strongly associated with prior SARS-CoV-2 infection. Activated CD4+ and CD8+ T cell responses were evident in most patients, with wide variation, irrespective of COVID-19 history. Further studies are needed to determine whether these activated CD4+ and CD8+ T cell responses were antigen-specific or confer immunity.

Table 1: Patient Demographics

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>N</td>
<td>49</td>
</tr>
<tr>
<td>Mean Age (y) (SD)</td>
<td>54 (11)</td>
</tr>
<tr>
<td>Male − n (%)</td>
<td>39 (79.6)</td>
</tr>
<tr>
<td>Race − n (%)</td>
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<tr>
<td>Black</td>
<td>22 (44.9)</td>
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<tr>
<td>White</td>
<td>15 (30.6)</td>
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<td>Asian</td>
<td>2 (4.1)</td>
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<tr>
<td>Other</td>
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<td>Multiple</td>
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</tr>
<tr>
<td>Time since transplant (y) − mean (SD)</td>
<td>2.2 (6.2)</td>
</tr>
<tr>
<td>Induction Agent</td>
<td></td>
</tr>
<tr>
<td>Basiliximab</td>
<td>19 (38.8)</td>
</tr>
<tr>
<td>Anti-thymocyte globulin</td>
<td>30 (61.2)</td>
</tr>
<tr>
<td>Maintenance IS regimen</td>
<td></td>
</tr>
<tr>
<td>CNI-based</td>
<td>44 (89.8)</td>
</tr>
<tr>
<td>Belatacept-based</td>
<td>5 (10.2)</td>
</tr>
<tr>
<td>Prior SARS-CoV-2 infection − n (%)</td>
<td>15 (30.6)</td>
</tr>
</tbody>
</table>
246.2

**Novel Avenue of Allograft Monitoring: Direct Measurement of Donor-Derived Extracellular Vesicles in Human Plasma**

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**Background:** Extracellular Vesicles (EVs) - regarded as “snapshots” of their cell of origin - represent promising liquid biomarkers to monitor allograft function post-transplantation. Recently, we developed an imaging flow cytometry (IFCM) based protocol to identify and characterize EVs ≤400 nm in molecularly complex samples such as human plasma without prior isolation of EVs. Using this protocol, we measure allograft derived EVs based on HLA phenotype as a first step to detect allograft specific EVs in the circulation of kidney transplant (KTx) recipients.

**Materials & Methods:** EDTA blood samples from kidney transplant donors (HLA-A2+, n=21) and recipients (HLA-A2-, n=33) were collected before transplantation as well as 3 days, 7 days, 6 months and during “for-cause” biopsies (recipients only) after transplantation. Platelet-poor plasma (PPP) was stained with a donor-specific HLA antibody (HLA-A2) in combination with a common EV marker (tetraspanin CD9) and measured using standardized IFCM.

**Results:** Quantification and comparison of CD9+/HLA-A2+ double-positive EV showed 1.1E± ± 8.9E vs 3.5E± ± 2.5E objects/mL for donor and recipient (pre-KTx) EVs respectively, with recipients A2- EVs concentrations representing background level of the machine. CV values for inter- and intra-assay variability were 16% and 11%, respectively. Serial dilution of A2+ PPP in A2- PPP (n=5) showed a linear reduction in the numbers of CD9+/HLA-A2+ EVs according to the dilution rate whilst total CD9+ EV levels remained unchanged. The lower limit of detection of our protocol was defined as the dilution at which point CD9+/HLA-A2+ EVs dropped below baseline (A2-PPP), and was determined to be ~1% of the concentrations measured in undiluted A2+PPP (Figure). Measurement of longitudinally collected recipient samples revealed the detection of allograft derived EVs as soon as 3 days – but up to at least 6 months – after KTx.

**Conclusion:** Here we demonstrate for the first time the detection of allograft derived EVs in the circulation of KTx recipients in unprocessed human plasma samples. Identification, quantification and characterization of these EVs opens up the possibility to monitor these EVs over time after transplantation, and may prove to be a minimally-invasive biomarker.

246.3

**MicroRNA Tests for Complex Diagnostic of Acute Rejection And Bacterial Infection After Heart Transplantation**

Sofya Sharapchenko1, Olga Shevchenko1,2, Dmitry Veliky1, Olga Gichkun1,3, Vitaly Poptsov2, Natalya Mozheiko2, Nina Gabrielyan4, Alex Shevchenko3,5, Sergey Gautier6,7.

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**Introduction:** The acute rejection and bacterial infections are the main risk factors of primary graft dysfunction and high mortality after heart transplantation (HTx). The search for new minimally invasive diagnostic methods and biomarkers of graft damage is extremely relevant. MicroRNAs are widely known as small molecules, regulating gene expression. Some of them (miR-27, -101, and -424) are involved in the mechanisms of cardiovascular diseases. The aim of the study is to determine the diagnostic value of miR-27, miR-101 and miR-424 levels for early post-transplant complications – heart graft acute rejection and gram-negative bacterial infections.

**Methods:** The study enrolled 83 heart transplant recipients, aged 16 to 70 (48.6±10.9) years. The expression levels of miR-27, -101, and -424 were measured by PCR (Qiagen, USA) in plasma after HTx. Graft rejection was verified through morphological analysis of endomyocardial biopsy specimens: infection – through microbiological identification in blood culture.

**Results:** The miR-424 level didn’t differ (p=0.47) in recipients with (n=39) and without acute graft rejection (n=44), however miR-27 and miR-101 levels are significantly lower in recipients with acute graft rejection than in recipients without (p=0.01 and p=0.02 resp.). By the way the diagnostic value of miR-27 and -101 and its threshold value for heart transplant acute rejection was found: when miR-27 expression level is below threshold value the relative risk of acute rejection is RR=1.8 [95% CI 1.13–3.01]; miR-101 – below threshold value RR=1.9 [95% CI 1.13–3.37]. For miR-27 the sensitivity (Se) and specificity (Sp) were 53.6% and 79.2%; for miR-101 – 64.3% and Sp=70.8% resp. (Fig. 1).

**Conclusion:** The measurement of miR-27, -101, and -424 expression levels can be used as complex tests for monitoring the risk of acute rejection and bacterial infections after HTx.
Myocardial Fibrosis in Heart Transplant Recipients Is Associated With the RS1800470 Polymorphism of the TGFβ1 Gene

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Introduction: Myocardial fibrosis is one of the factors that have a negative impact on long-term prognosis after heart transplantation. Its development is most often accompanied by a violation of the structure and function of the cardiac allograft in recipients. Transforming growth factor β1 is a pleiotropic cytokine involved in the formation of fibrosis. Single nucleotide polymorphisms in the regulatory regions of the TGFβ1 gene affect the level of expression and, accordingly, mediate various biological effects of the encoded protein.

The aim: to estimate polymorphisms rs1800469, rs1800470, rs1800471 of the TGFβ1 gene and their relationship with myocardial fibrosis in heart transplant recipients.

Materials and Methods: 110 heart transplant recipients were examined, including 99 (84%) men; the average age of the recipients was 44±14 (from 16 to 70) years. Polymorphisms rs1800469, rs1800470, rs1800471 of the TGFβ1 gene were determined using real-time polymerase chain reaction (TaqMan probes). Fibrosis of the cardiac allograft was verified by the results of endomyocardial biopsy; thin sections of endomyocardial tissue were stained with Masson’s trichrome.

Results: In 49 heart transplant recipients with verified fibrosis, the following distribution of the studied polymorphisms was observed: rs1800469 - 11% AA homozygotes, 35% AG heterozygotes, and 54% GG homozygotes; rs1800470 - 98% AA homozygotes, 2% AG heterozygotes, and 0% GG homozygotes, rs1800471 - 0% GG homozygotes, 2% GC heterozygotes and 98% CC homozygotes. In heart transplant recipients without fibrosis: rs1800469 - 25% AA homozygotes, 46% AG heterozygotes and 29% GG homozygotes, rs1800470 - 82% AA homozygotes, 11% AG heterozygotes, and 7% GG homozygotes, rs1800471 - 100% CC homozygotes. There were no differences in the distribution of genotypes and alleles of investigated polymorphisms TGFβ1 gene in recipients with and without fibrosis.

Conclusion: The presence of the AA rs1800470 genotype of the TGFβ1 gene in heart transplant recipients may be associated with a predisposition to the development of graft myocardial fibrosis.
How Much Is Too Much? Determining the Optimal Oxygen Concentration for Early Hypothermic Oxygenation of Liver Grafts in Rodents

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Introduction: Ischaemia is inevitable during organ preservation and contributes to graft dysfunction after liver transplantation. Early oxygenation of grafts during organ preservation, such as oxygenated washout (OW), has been shown to reduce ischaemic injury. However, the optimal oxygen concentration for OW is unknown. Hyper-oxygenation can induce reactive oxygen species and graft injury. This study compared non-oxygenated preservation with moderate and high oxygen concentrations during OW in rat livers.

Methods: Donation after circulatory death livers were procured from 10 rats. Grafts were randomised to three groups: control (non-oxygenated University of Wisconsin Solution (UW)), moderate concentration OW (Mod-OW) (25-28mg dissolved oxygen/L) and high concentration OW (High-OW) (>50mg dissolved oxygen/L). Livers were flushed and stored at 4°C. After 24 hours of cold storage, livers were placed on isolated liver-reperfusion (ILRP) for 120 minutes. Dissolved oxygen in preservation fluid was measured throughout cold storage. Tissue ATP, as a marker of graft viability, was measured at 0, 6 and 24H cold storage, and after ILRP. Liver biochemistry and graft oxygen consumption were measured during ILRP.

Results: The control group had lower dissolved oxygen in the preservation fluid than OW groups at 0H and 6H (all p<0.05) (Figure 1A-B). Tissue ATP was similar between groups at 0H. By 6H, grafts in the Mod-OW group had greater tissue ATP than the High-OW group (15.7 vs 8.4 ug/mg, p = 0.01) (Figure 1C). After 24H cold storage, preservation fluid oxygenation and tissue ATP were similar between all groups.

During 120 minutes ILRP, the mean oxygen consumption of the Mod-OW group was greater than the High-OW group (47.2 vs 24.4 uL/min/g-liver, p = 0.048) (Figure 1D). No difference in liver biochemistry was observed (Figure 1E-F).

Conclusion: Rat livers receiving Mod-OW had increased tissue viability at 6H and oxygen consumption on ILRP compared to High-OW. Our findings suggest that high oxygen concentrations may lead to reduced graft viability. Although OW may be beneficial for organ preservation, oxygen concentrations should be closely monitored to prevent hyper-oxygenation.
Long-term Rejection Free Renal Allograft Survival With Fc-Modified Anti-CD154 Antibody Monotherapy in Nonhuman Primates

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1Center for Transplantation Sciences, Massachusetts General Hospital, Boston, MA, United States.

Belatacept is currently an only FDA approved costimulatory blockade (CB) used as an alternative to calcineurin inhibitors in kidney transplantation. However, it has been associated with higher rates of acute cellular rejection (ACR) and more effective CB has been sought. Blockade of the CD154/CD40 pathway with anti-CD154 antibody (aCD154) has been shown to be more effective in inhibiting alloimmune responses than CTLA4ig. Unfortunately, clinical application of aCD154 has been abandoned due to its thrombophilic property which appears to be mediated by FcγRIIa receptor–dependent platelet activation. To address this problem, an Fc-modified aCD154 (TNX-1500), in which Fc was engineered to decrease binding to FcγRII, has been developed. In the current study, we have evaluated TNX-1500 for its efficacy to prevent kidney allograft rejection in NHPs.

Twelve cynomolgus macaques received MHC mismatched kidney allografts with either TNX-1500 monotherapy (20mg/kg weekly) (Group A) or combined with daily mycophenolate mofetil (MMF) (TNX-1500 weekly for 6 weeks followed by every 2 weeks) (Group B). The results were compared with our historic results of no immunosuppression (No IS, n=5) or conventional immunosuppression (I.S.) with tacrolimus (Tac), MMF and methylprednisolone (Pred). (Conventional IS, n=20).

Without any prophylaxis, no thromboembolic complication was observed in all nine recipients of TNX-1500. Renal allograft survival at 6 month was 80% in Group A (n=6). Histopathology at 6 months of 5/6 recipients showed no evidence of rejection (g0,i0,t0,v0,pxc0,cfg0,c0,c0,c0,c0,v0). One recipient lost on day 28 with ACR2b. Six recipients have so far have been tested in Group B. Two recipients developed rejection on day 36 and 48 while they were still treated with weekly TNX-1500. Another recipient had to be euthanized on day 111 post-transplant due to complications from MMF. The three other recipients in this group are currently in progress with normal kidney function at days >180, >84 and >42. Renal allograft survival at four months in Conventional I.S. was 52% (p=0.03 vs. Group A) and all five recipients without I.S. rejected their kidney allografts by day 11 (p=0.0018 vs. Group A). Excellent renal allograft survival was achieved with TNX-1500 monotherapy without thromboembolic complications. Combination with MMF resulted in inferior allograft survival.

Renal Allograft Survival

<table>
<thead>
<tr>
<th>Group</th>
<th>TNX-1500</th>
<th>MMF</th>
<th>Tac</th>
<th>Pred</th>
<th>Renal allograft survival (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A weekly</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>&gt;180, &gt;180, &gt;180, &gt;180, &gt;77, 25</td>
</tr>
<tr>
<td>B weekly for 6 weeks, followed by every 2 weeks</td>
<td>- daily</td>
<td>daily</td>
<td>daily</td>
<td>&gt;120, &gt;120, &gt;120, &gt;120, &gt;120, &gt;120, &gt;120, &gt;120, &gt;114, &gt;106, &gt;84, &gt;68, &gt;65, 55, 43, 27</td>
<td></td>
</tr>
<tr>
<td>Conventional I.S.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>11, 10, 9, 8</td>
</tr>
</tbody>
</table>

Financial support from NIH Grants 1R21AI163806-01, 5T32AI007529-22 & Tonix Pharmaceuticals.
High Alemtuzumab Exposure Is Associated With Delayed Lymphocyte Recovery in Kidney Transplant Recipients

Suzanne Bezstarosti1,2, Tom C. Zwart3, Federica R. Achini4, Marco W. Schilham5, Dirk Jan A. R. Moes5, Marlies E. J. Reinders6, Johan W. de Fijter2, Sebastiaan Heidt2,5.

1Immunology, Leiden University Medical Center, Leiden, Netherlands; 2Internal Medicine (Nephrology), Leiden University Medical Center, Leiden, Netherlands; 3Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, Netherlands; 4Paediatrics, Leiden University Medical Center, Leiden, Netherlands; 5Eurotransplant Reference Laboratory, Leiden, Netherlands.

Background: While alemtuzumab is increasingly being used as an induction therapy in kidney transplantation, little is known about the relation between alemtuzumab exposure, lymphocyte recovery and clinical outcomes in kidney transplant recipients (KTRs). Recently, a population pharmacokinetic model was developed based on alemtuzumab plasma concentrations of KTRs in the Triton Study, which allows for estimation of individual alemtuzumab pharmacokinetics. We hypothesized that alemtuzumab exposure would demonstrate substantial interpatient variability and correlate with lymphocyte recovery rate and infection incidence post-transplantation (post-Tx).

Methods: KTRs in the control arm of the Triton Study (n=29) were included in this analysis. All patients received alemtuzumab induction (2x 15 mg subcutaneously), steroids, tacrolimus and everolimus. As previous studies have suggested that alemtuzumab has lympholytic capacity at concentrations exceeding 0.1 mg/L, the time above this threshold concentration (TATC) and the maximum concentration (Cmax) were predicted using a validated population pharmacokinetic model. Immune monitoring of lymphocyte subsets was performed at baseline and at week 6, 12, 24, 52 and 104 post-Tx. CD4 T cell recovery was defined as > 50,000 CD4 T cells/ml peripheral blood, as counts below this limit have been associated with a higher risk of viral reactivation.

Results: The predicted TATC and Cmax demonstrated considerable interpatient variability ranging from 29.9-64.0 days (median: 39.7) and 0.54 to 1.39 mg/L (median: 0.80) respectively. KTRs with a TATC > 66th percentile (42.4 days) were categorized as ‘high exposure’ and patients below this threshold as ‘low exposure’. Median absolute CD4 T cell numbers at week 6 (118 vs 443, P=0.0096) and week 12 (1519 vs 7762, P=0.003) were lower in KTRs with high exposure than in patients with low exposure. Similar trends were observed for CD8 T cells, regulatory T cells and to a lesser degree for B cells. In order to predict the timepoint that patients reached CD4 T cell recovery more accurately, time to CD4 T cell recovery for every patient was predicted using a basic, empirical nonlinear mixed effects model. Kaplan Meier analysis demonstrated that KTRs with high exposure reached CD4 T cell recovery at later timepoints than patients with lower exposure (Figure 1). Regardless of differences in lymphocyte recovery rate, there was no statistically significant difference in the cumulative incidences of BK-virus, CMV, EBV or de novo donor-specific antibody formation between the two groups.

Conclusions: Alemtuzumab exposure demonstrates extensive interpatient variability and impacts lymphocyte recovery rate early after transplantation. Personalized dosing strategies could possibly limit interpatient variability in alemtuzumab exposure and subsequently lymphocyte recovery rate, but further research is warranted to study the potential clinical benefit.

References:
Effect of GLP-2 Analogue on Intestinal Ischemia-Reperfusion Injury in Mice: Initial Results

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Introduction: In recent years it has been shown that ischemia-reperfusion injury (IIR) is one of the risk factors associated to graft rejection. In the intestinal graft, the loss of the mucosal barrier function, the alteration in the permeability and structure of the villi are directly caused by IIR, mainly during the reperfusion process. Glucagon-like peptide-2 (GLP-2) is an intestinal hormone secreted by enteroendocrine L cells of the intestinal epithelium, the main therapeutic use of GLP-2 has been intestinal adaptation, but few experimental studies have shown a role in decreasing inflammatory damage. Therefore we had hypothesized a possible protective effect of GLP-2 to reduce intestinal IIR in a mice model.

Methods: The study was approved by the internal review board and ethics committee for the care and use of laboratory animals (CICUAL UF 2019-004, #PICT 2016-3677). An IIR model clamping the superior mesenteric artery for 40 minutes followed by 30 minutes of reperfusion was proposed as control group. Five experimental lines has been performed: 1) Sham Group, 2) Sham Group with intraperitoneal GLP-2 pretreatment for 3 days before surgery and an intraoperative dose (Sham+GLP2), 3) IIR Control Group, 4) IIR Group with intraperitoneal GLP-2 pretreatment for 3 days before surgery and an intraoperative dose (Pret-GLP2) and 5) IIR Group with only one intraoperative dose of GLP-2 (Intra-GLP2). After the reperfusion period, the mice were sacrificed and serum, intestine, liver and lung samples were taken. Histopathology and quantification of intestinal and pulmonary damage were performed. Park score was used for intestinal histological analysis. One-way ANOVA, and Kruskal-Wallis test were used.

Results: Sham groups (1 and 2) and study groups (4 and 5), showed significantly less intestinal injury compared to the Control group (3). The group with only one intraoperative dose of GLP-2 (5), had less average damage than the group with pretreatment and an intraoperative dose of GLP-2 (4). The damage evaluated in the lung presented significant differences between the Sham groups (1 and 2) and the Control group (3). Although the IIR group with intraoperative administration of GLP-2 showed the least histological lung damage of all groups under IIR, there were no significant differences between these preliminary results.

Conclusion: A marked decrease in IIR damage of intestine was observed by using GLP2 as pretreatment or intraoperative intraperitoneal. These preliminary results prove the hypotheses; the use of GLP2, to reduce IIR, opens a new line of research and potential new clinical use.
Conditional Altruistic Living-Donor Kidney Donation in Israel and Its Impact on Living-Donor Kidney Transplant Growth

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Introduction: With a limited number of deceased organ donors in Israel, transplant tourism was often used as an alternative source for kidneys until the enactment of the Israel Transplant law in 2008 which severely limited that activity. In an effort to find a legitimate path for the supply of kidneys for transplant, the law approved altruistic donation and established a regulated central governmental mechanism to ensure an altruistic motivation for donation. A year later, in 2009, the Matnat Chaim organization started its initiative to promote altruistic donation within the Jewish sector according the highest imperative of saving another’s life according to religious beliefs and social behaviour. Here, we report the results of that activity over the last 8 years.

Methods: We used Israel Transplant Centre database and the Matnat Chaim organization’s database reporting the transplant activity for the period of 2013-2021. We looked at the growth of deceased and living-donor kidney transplantation and the proportion of altruistic kidney donations out of the total number of living-donor transplants over that period. We also reviewed the donors’ pre-donation questionnaire and their preferences regarding their paired recipients in terms of age, social sector, and religious observance.

Results: Over the period studied, the number of kidney transplant candidates on the waiting list increased from 755 to 917 patients while the number of kidney transplants from deceased donors increased from 127 to 149 (excluding combined kidney-liver or kidney-pancreas transplants). The total number of live-donor transplantation increased from 261 to 476. The primary growth in the number of kidney transplants came from altruistic donations, with an increase from 32 to 215 donors a year (6.7%), and their proportion within the overall live donor total increased from 24 to 66% (figure 1). It should be noted that in many cases, Matnat Chaim was responsible for facilitating donation within the family after an initial interview of patients who approached the organization. Although in the majority of cases altruistic donors donated their kidney to a recipient within their community or religious group, on other occasions donors agreed to change the original directed allocation and donate their kidney within a paired exchange program (48 donors) or directly to a highly sensitized patient on the waiting list. However, for many of the altruistic donors, conditional donation was a prerequisite and had they not been allowed to donate within their community, they would not have donated a kidney at all.

Conclusions: Conditional altruistic donation within a community is a legitimate path with a major potential to increase organ donation. Unlike non-conditional donation where kidneys are allocated to the waiting list, our system of conditional altruistic donation may raise some ethical issues; however, we consider it a valid option on a scale between a family donation and altruistic non-directed donation. The abstract is in memory of my friend Rabbi Yeshayahu Heber, the founder and chairman of Matnat Chaim. Rabbi Heber was a transplant recipient who died far before his time during the first wave of the COVID-19 pandemic, in April 2020. Over 1200 kidney recipients are alive today due to his vision and determination.
247.3

Utility of Liver Biopsy in Liver Transplantation: Implications for Changes in Liver Allocation

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Introduction: Histological evaluation of a potential donor liver can provide useful information prior to liver transplantation (LT) and potentially reduce discard rates. However, the use of a liver biopsy (LB) is not standardized across Organ Procurement Organizations. On February 4, 2020, the LT allocation policy in the United States changed, likely shifting institutional and regional behavior changes for the acceptance of donated organs. We sought to review LB utilization patterns before and after the institution of the acuity circle allocation system (ACAS) and determine if LB rates were associated with allograft discard rates, patient and graft survival.

Methods: Data from the Scientific Registry of Transplant Recipients (SRTR) were analyzed on the utilization of LB before and after the implementation of ACAS. Era 1 was defined as January 1, 2018 to February 3, 2020; Era 2 was defined as February 4, 2020 to June 1, 2021. Statistical comparisons between eras were performed. Univariable and multivariable models were constructed to determine donor characteristics that were correlated with obtaining a LB during the eras. Kaplan-Meier survival analysis was performed to determine the impact of LB on patient and graft survival.

Results: We analyzed 29,905 liver transplants performed from January 1, 2018 to June 1, 2021; 17,949 (60%) were performed in Era 1 and 11,956 (40%) were performed in Era 2. During the study time period, there were 11,043 LB performed; 6,488 (58.8%) in Era 1 and 4,555 (41.2%) in Era 2 (p<0.001). Era 1 demonstrated a LB rate of 36.1% while Era 2 demonstrated a LB rate of 38.1% (p<0.001). Donor characteristics associated with obtaining a LB were BMI, race, age, history of DM, and era. The discard rate between Era 1 (15.8%) and Era 2 (15.0%) did not differ (p=0.097). The 1- and 3-year patient survival for LT recipients was 93.3% and 83.5%, respectively. The 1-year patient survival for LT recipients during Era 2 was 89.9% and graft survival was 96.1%.

Conclusion: The institution of the ACAS led to differing acceptance practices around liver transplantation. In the time period after institution of the model, there was a statistically significant increase in utilization of LB, likely due to wider catchment areas for potential recipients. ACAS seemed to have no effect on the rates of allograft discard rates, patient, or graft survival.

247.4

Can Ex-vivo Normothermic Perfusion Improve Graft Survival Compared to Static Cold Storage Among DCD Liver Allografts?

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Introduction: Limited data suggests that ex-vivo normothermic liver perfusion (ENLP) may improve the outcomes of donation after cardiac death (DCD) liver transplants compared to static cold storage (SCS).

Methods: All adult, DCD liver transplants performed between 2016-2021 were identified in the United Network of Organ Sharing (UNOS) database. Cox proportional hazards analysis was used to evaluate the impact of ENLP (vs SCS) on graft survival. To more effectively balance baseline covariates and minimize treatment selection bias, an inverse probability of treatment weighting (IPTW) approach using the propensity score was employed, which accounted for multiple donor and recipient factors.

Results: Between 2016 and 2021, 65 ENLP and 3079 SCS DCD liver transplants were performed in the U.S. Only 20/101 centers utilized ENLP DCDs. Compared to SCS DCDs, recipients of ENLP DCDs had lower MELD scores at transplant (16.5 v. 18.8, P=0.033), longer wait-times (468±720 v. 246±467 days; P<0.001), and received livers from donors with a greater BMI (29.2 v. 27.5; P=0.008). ENLP preservation was associated with improved graft survival (HR 0.15 vs SCS, 95% CI:0.04-0.60, P=0.01). As a majority of the ENLP DCDs were performed in the context of multicenter trials, we conducted a sub-analysis restricting to the 20 centers performing ENLP, encompassing 946 SCS DCDs. Results were largely unchanged: HR 0.16 vs SCS (95% CI: 0.04-0.62, P=0.01).

Conclusion: In this retrospective analysis of the early U.S. DCD ENLP experience, there may exist a graft survival benefit to transplants performed with ENLP compared to SCS. Future analyses will require a more robust dataset with longer-follow-up.
Magnetic Resonance Imaging of Renal Oxygen Metabolism by Means of 17-O Administration During Ex Vivo Organ Perfusion

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Background: Renal normothermic machine perfusion (NMP) is a method studied for pre-transplant evaluation of kidney graft quality. This technique creates an isolated near-physiological environment by circulating a perfusion solution at body temperature with oxygen and nutrients. However, reliable ex vivo organ viability markers are still lacking. Magnetic resonance imaging (MRI) has recently been applied as a new rapid non-invasive technique to study renal viability ex vivo. Oxygen-17 (17O) offers a novel sensitive assessment of oxidative metabolism. In our MRI compatible perfusion setup, we aimed to study oxygen metabolism during NMP.

Methods: Three viable porcine kidneys were retrieved at a slaughterhouse and preserved by oxygenated hypothermic machine perfusion. In addition, one discarded human kidney was shipped to our center in static cold storage. Subsequently each kidney was perfused for 4 hours at 37°C inside a clinical 3T MRI scanner. Blood gas, glucose, and electrolytes were periodically monitored. Anatomical T2-weighted images and T2* maps were obtained using a 1H 18Ch-bodyflex coil and dynamic radial 17O MR images were acquired using a 17O Tx/Rx loop coil and a 17O 3D-UTE sequence. The 17O perfusion protocol consisted of 4 minutes of deoxygenation with nitrogen gas, 8 minutes of 70%-enriched 17O2 gas infusion at 0.1L/min, and 20 minutes of subsequent carbogen (95% O2/ 5% CO2) oxygenation. 17O-magnitude data was analyzed dynamically over time. To study the 17O-related global signal change, a region of interest was defined in the anatomical T2-weighted images and co-registered to the dynamic 17O-magnitude data.

Results: Porcine kidneys showed homogenous perfusion with increased H217O-concentration in the medulla and decreased concentration in the cortex. The discarded human kidney demonstrated a focused concentration in the medial side of the lower pole with little to no signal intensity in the upper pole and the majority of the cortex, which was consistent with its reason for discard (wide cist in the lateral pole).

Six minutes after administration of 17O2-gas, a rapid H217O signal increase was observed until minute 20 of the dynamic acquisition, where saturation was reached and the signal plateaued. Overall, an enhancement of 16% between the first and last data point was measured.

Conclusion: In these pilot experiments, we were able to quantify the regional production of H217O in time, both in porcine and human kidneys. The slope of occurrence of H217O may be an interesting ex vivo organ viability biomarker, immediately related to the rate of oxidative metabolism in the organ and hence organ quality. As the kidney is in an ex vivo setting, any increase in H217O-concentration must be the direct result of metabolism within the organ. The current setup has great potential for investigating renal oxygen metabolism ex vivo.

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Preliminary Results of Ex-vivo Normothermic Machine Perfusion in Deceased Donor Renal Allograft Transplantation – First Clinical Experience From Asia

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Introduction: In India, less than 5% of the ESRD population receive a kidney transplant. This prevailing shortage led to increased acceptance of kidneys from high-risk donors, e.g., the donor with acute kidney injury (AKI) and donation after uncontrolled circulatory death donors (uDCD). Application of Normothermic machine perfusion (NMP) can assess the functional viability of these grafts and can hasten early functional recovery after transplantation. However, literature regarding NMP application in kidney transplantation remains limited. We present our early preliminary experience with the usage of NMP in kidneys procured from deceased organ donors with successful kidney transplantation and describe their short-term outcomes.

Methods: Between December 2019- July 2021, consented recipients were eligible for inclusion if they had received AKI or uDCD grafts. Donor’s kidneys underwent a two-hour of oxygenated NMP (based on Cambridge clinical trial protocol) with a red cell-based solution at 37°C after retrieval in addition to static cold storage (SCS). The main indication for NMP was to reduce the DGF amongst the AKI kidneys and organ viability assessment amongst the uDCD kidneys.

Results: Seven kidneys were transplanted into seven recipients after NMP (5 DBD+ 2 uDCD [one en-block neonatal kidney]). The third uDCD was discarded based on prolonged functional warm ischemia time (>2hrs) and poor, patchy perfusion on NMP. The primary function was observed in six recipients, and four had DGF. One recipient of uDCD kidney had graft loss due to invasive aspergillosis at 3-month post-transplant other six recipients are doing well with a baseline creatinine of (0.8-1.1mg/dl) on follow-up (12-22 months) without any rejection episodes.

Conclusions: This pilot study showed the feasibility and utility of NMP in pretransplant reconditioning and viability assessment amongst AKI and uDCD grafts. NMP has the potential to increase the organ donor pool.

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Trends and Risk Factors for Mortality While Awaiting Heart Transplantation: A UNOS Registry Analysis

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Background: Orthotopic heart transplantation (OHT) remains the gold standard treatment of end-stage heart failure. In order to address organ scarcity, allocation systems aim to decrease waitlist mortality while maintaining acceptable post-transplant outcomes. The purpose of this study was to examine the characteristics of patients who suffered mortality on the waitlist versus those who underwent transplantation, as well as the impact of recent changes in the United States heart allocation policies on these outcomes.

Methods: The United Network for Organ Sharing database was queried, and adult, isolated OHT candidates listed for transplant within the United States from 11/5/2015 to 9/30/2021 were analyzed. Baseline characteristics among candidates that either were transplanted, or had been removed from the waitlist due to death clinical deterioration were compared. Comparisons were also made between heart allocation policy (pre or post-10/18/2018) time eras. Multivariable competing risk regression was conducted to identify risk-adjusted predictors of transplantation from the waitlist. Additionally, predictors of the outcome of death or de-listing from the waitlist due to clinical decline were also modeled.

Results: During the study period, a total of 13,575 recipients were transplanted (6,926 under the old policy and 6,649 under the new). A total of 1,875 candidates died or were de-listed (1,235 listed under the old policy and 640 listed under the new). In a comparison of baseline characteristics at time of listing, candidates that were transplanted differed significantly to those who were de-listed due to death or clinical decline with respect to age, heart failure etiology, mechanical circulatory support bridging, and baseline comorbidity (Table). In a multivariable model, waitlisting under the new allocation policy was associated with reduced hazards for death or de-listing (HR 0.57, 95% CI 0.51-0.63; P<0.001), and increased hazards for undergoing transplantation (HR 1.36; 95% CI 1.31-1.41; P<0.001). The two largest predictors of transplantation were being bridged with an intra-aortic balloon pump (HR 2.13, 95% CI 1.97-2.31; P<0.001) and AB blood type (HR 1.43, 95% CI 1.30-1.57; P<0.001). The strongest predictors of death or de-listing were diagnosis of hypertrophic cardiomyopathy (HR 3.77, 95% CI 2.69-5.29; P<0.001) or biventricular hemodynamic support in the form of either extra-corporeal membrane oxygenation (HR 2.59, 95% CI 1.96-3.42; P<0.001), total artificial heart (HR 2.36, 95% CI 1.28-4.35; P=0.006), or combined right and left ventricular assist device support (HR 2.45, 95% CI 1.71-3.50; P<0.001).

Conclusions: Since the United States 2018 heart allocation policy change, waitlisted candidates are more likely to be transplanted and less likely be de-listed due to death or clinical decline. Need for biventricular mechanical circulatory support at time of waitlisting are associated with higher risk of death or falling too ill for transplantation.
247.8

Early Experience of 48-Hour Normothermic Machine Perfusion in Human Kidneys Applying Urine Recirculation

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Introduction: Normothermic machine perfusion (NMP) of the kidney has been studied extensively during the past decade. Short-term kidney NMP has demonstrated promising results, however currently transplant logistics cannot be improved and for organ treatment longer preservation periods might be necessary. As a proof of principle, we aimed to achieve 48-hour NMP by applying urine recirculation (UR) with a commercially available perfusion device.

Methods: Discarded human kidneys were normothermically perfused on the XVIVO Kidney Assist perfusion device. The perfusate comprised packed red cells and 5% albumin. For volume management UR was applied. Air (21% O2) and CO2 were used for oxygenation of the circuit and monitored with an in-line blood gas analyzer. Perfusate and urine samples as well as hemodynamics were regularly assessed.

Results: Five discarded human kidneys underwent kidney NMP following hypothermic machine perfusion (HMP) and static cold storage. All but one kidneys were DBD organs. Median donor age (range) was 62 (41-68) years. Median (IQR) CIT and HMP were 19.9 (12.1) h and 5 (7.2) h. An NMP duration of 48 h could be achieved in all kidneys. All kidneys were urinating throughout with a median (IQR) output of 22.5 (30.5) ml/h. Overall median (IQR) arterial flow was 695 (383) ml/min. Median (IQR) pH was 7.2 (0.2). Overall median (IQR) perfusate sodium, chloride and potassium were 161 (14.7) mmol/L, 124.5 (11.5) mmol/L, and 6.5 (2.7) mmol/L. Median (IQR) perfusate sodium was significantly higher than corresponding urine values (sodium: 130 (27) mmol/L, chloride: 120.5 (11.8) mmol/L) over time (P = 0.02 and 0.04). Median arterial flow over time was significantly higher in NMP kidneys with lower perfusate sodium levels (p<0.001, correlations coefficient Spearman’s rho -0.461).

Conclusions: This early experience underlines the feasibility of extended ex situ kidney NMP by applying UR. Hemodynamic stability and urine excretion were achieved for 48 hours.

247.9

Liver Transplantation from Discarded Liver Grafts. A Useful Policy for Expanding the Liver Donor Pool in Mexico

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Background: Extended criteria donors (ECD) in liver transplantation (LT) is gaining worldwide acceptance due to the shortage of optimal donors. Most of liver transplant groups agree that age over 60, prolonged cold ischemia time (CIT), steatosis, inotropic support, non-heart beating donors (NHBD), sustained hypernatremia, split livers among other factors are related to primary non-function (PNF) with high morbimortality. Before COVID-19 pandemia discarded liver grafts that nobody wants accounts for the double of LT done each year in Mexico and it seems that there is an increasing rate of marginal or ECD. To define discarded liver grafts, these must be refused by 3 of the main liver transplant centers in the country and have ≥ 3 risk factors for PNF and delayed graft function (DGF).

Method: A period from January 2015 to January 2021 was observed. Donor characteristics such as sustained severe hypernatremia (>165 mEq/l), moderate steatosis (>40%), body mass index (BMI) >30 k/m2, alcohol abuse, CIT >12 h and norepinephrine support among others were considered risk factors for PNF and DGF. Morbidity and mortality were evaluated.

Results: 159 LT were done. Marginal donors 61 (38.3%), discarded livers 40 (65.5%). Severe hypernatremia (165-188 mEq/l) 20 (50%), obesity (BMI 30-45k/m2) 30 (75%), moderate steatosis (40-76%) 22 (55%), alcohol abuse in 3 (7.5%), age >60 (35%) and norepinephrine support 27 (67%). No CIT >12 h was recorded. PNF between marginal and discarded liver grafts were the same (5%) and between optimal grafts and discarded or marginal the rate of PNF were 2.1 to 5%. DGF was present in 7.5%, 5% and 3.1% of discarded, marginal and optimal grafts respectively (Table 1). No differences in mortality rate between groups.

Conclusion: Discarded livers are an acceptable choice to expand liver donor pool in Mexico. None hypernatremia, obesity, steatosis or age are independent poor risk factors for developing PNF.
Abstracts

247.10

Controlling Instability at Reperfusion: Another Benefit of Normothermic Machine Perfusion Using OCS Liver

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Introduction: Organ Care System (OCS) Liver is a portable ex-vivo normothermic liver perfusion device recently shown to provide superior donor organ preservation. The impact of OCS Liver on post-reperfusion syndrome (PRS) remains unknown.

Method: This was a retrospective, single center, case-control study. All transplants utilizing OCS Liver between 1/1/2018 and 12/31/2020 were compared with a propensity score matched (PSM) cohort. The control population was matched for age, MELD, donor type and ventilator/circulatory support. Multiorgan transplants were excluded from the analysis. Donor, procurement, and recipient characteristics were collected for all recipients. Anesthesia records containing vitals by minute and pressor/inotropes were collected to establish baseline (5 minutes prior to reperfusion) and up to 30 minutes post-reperfusion hemodynamics.

Results: Following PSM there were 97 liver transplants in the study cohort, including 38 OCS (39%) and 59 controls (61%). Donor and recipient characteristics confirmed these groups were well matched. PRS, defined by ≥1 minute of mean arterial pressure 30% below baseline, was significantly reduced in the OCS group (1/38(3%) vs. 14/45(24%), p=0.005). OCS patients required significantly less post-reperfusion support, where both total norepinephrine (64 μg vs. 100 μg, p=0.02) and total epinephrine (18 μg vs. 38 μg, p=0.02) infusions were reduced compared to controls. Patients with combined blood pressure instability and pressor support were more likely to develop early allograft dysfunction (EAD), (15/56(27%) vs. 0/38(0%), p=0.001). However, the use of OCS was associated with a 10-fold reduction in EAD (1/38(2.6%) vs. 14/56(25%), p=0.004).

Conclusion: Normothermic machine perfusion using OCS Liver reduces hemodynamic instability after reperfusion and also results in a significantly reduced incidence of EAD.

| Table. Donor and recipient characteristics of propensity score matched groups. |
|---------------------------------|------------|------------|-------|
| **Donor characteristics**       | Control (n=59) | OCS (n=38) | P-value |
| Age (years)                     | 7 (26%)    | 66 (79%)  | 0.55  |
| Gender (Female)                 | 22(37%)    | 16(42%)   | 0.66  |
| BMI (kg/m²)                     | 30 (29%)   | 30 (26%)  | 0.78  |
| Macrosteatosis (%)              | 9 (15%)    | 12 (31%)  | 0.99  |
| Donor Risk Index                | 1.6 (12%)  | 1.7 (16%) | 0.26  |
| Donor after Cardiac Death       | 7(12%)     | 6(16%)    | 0.58  |

| **Recipient characteristics**   | Control (n=59) | OCS (n=38) | P-value |
| Age (years)                     | 7 (26%)    | 7 (18%)   | 0.59  |
| Gender (Female)                 | 22(37%)    | 14(36%)   | 0.97  |
| BMI (kg/m²)                     | 29 (23%)   | 29 (23%)  | 0.67  |
| MELD                            | 24 (25%)   | 24 (25%)  | 0.08  |
| Operative characteristics       | Control (n=59) | OCS (n=38) | P-value |
| Total clamp time (hrs)          | 4.7 (5.2)  | 5 (5.8)   | 0.03  |
| Anastomosis time (min)          | 27 (26)    | 26 (27)   | 0.85  |

| Post-reperfusion support         | Control (n=59) | OCS (n=38) | P-value |
| Norepinephrine (μg)             | 100 (24%)    | 64 (26%)   | 0.02  |
| Epinephrine (μg)                | 36 (18%)    | 18 (9.5%)  | 0.02  |
| Post-reperfusion syndrome       | 14/56(24%)   | 1/38(26%)  | 0.005 |
| Early allograft dysfunction      | 14/56(26%)   | 1/38(26%)  | 0.004 |
The Effect of Different Nutrients on Mitochondrial Function During Long Term Incubation of Precision-Cut Kidney Slices

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Introduction: Marginal donor kidneys are more susceptible to ischemia-reperfusion injury (IRI). IRI causes the mitochondria to produce reactive oxygen species (ROS) after reintroduction of oxygen. To diminish production and deleterious effects of ROS, mitochondria should be preserved optimally between donation and transplantation. Normothermic machine perfusion (NMP) is increasingly explored to improve quality during preservation. One important question is how to provide metabolic support to kidneys during NMP and which nutrients are best to support mitochondrial energy production. To resemble NMP circumstances, we developed a precision-cut kidney slices model that can study the kidney on a cellular level. The aim of this study is to investigate the effect of different nutrients on mitochondrial function during incubation of precision-cut kidney slices.

Methods: Pig kidneys were procured at a local slaughterhouse. After 30 minutes of warm ischemia kidneys were perfused with oxygenated hypothermic machine perfusion for 3 hours. For the human kidney, a cortical peace was cut off and put on cold storage until arrival at the lab. Thereafter, precision-cut kidney slices (PCKS) were made and incubated for 24 or 48 hours in different incubation media. The basic incubation medium was Dulbecco's Modified Eagle Medium (DMEM) without glucose and pyruvate supplemented with ciprofloxacin (10 µg/mL) and fungizone (0,25 µg/mL). To the groups either glucose, glutamine and/or fatty acids were added (table 1). At zero, 24 and 48 hours, mitochondrial respiration, using the Oxygraph-2k, was assessed, in which the glycolysis (pyruvate and glutamate) and the beta-oxidation of fatty acids (C16-carnitine) were stimulated. Furthermore, mitochondrial energy status and injury markers in the incubation medium were analyzed.

Results: Mitochondrial respiration, in terms of the respiratory control ratio (RCR), after HMP is best when only glutamate is used to stimulate. Furthermore, mitochondria were better preserved after 48 hours with the addition of glucose, glutamine and fatty acids compared to no nutrients. No differences were seen between glycolysis or fatty acid stimulation.

Conclusion: Nutrient composition impacts mitochondrial function of precision cut kidney slices. These data pave the way to optimize the perfusion solution for NMP of marginal donors.

Table 1. Overview nutrients per group

<table>
<thead>
<tr>
<th>Glucose (mg/dL)</th>
<th>Glutamine (mM)</th>
<th>Fatty acids (1,5 mg/mL)</th>
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<tbody>
<tr>
<td>Control 1 Pig</td>
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</tr>
<tr>
<td>Control 2 Pig</td>
<td>-</td>
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<td>Experimental group 1 Pig</td>
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<td>Experimental group 4 Pig</td>
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<tr>
<td>Experimental group 5 Pig</td>
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Figure 1. Glycolysis stimulated mitochondrial respiration after 48 hours of incubation
External Audit as a Tool to Improve the Clinical Management of Brain Death in Intensive Care Units: National Experience

Paul Mizraji¹, Mario Godino¹

Introduction: External auditing is a common practice in organizations, carried out by external professionals looking for opportunities for improvement. Since 2016, the INDT has carried out external audits of 22 public and private Intensive Care Units (ICU) annually to optimize the diagnosis and communication of EM.

Methodology: Evaluates patients who have died in the ICU in person, selecting neurocritical patients to detect EM diagnosis/communication leaks. Prior to the visit, the institution is asked to audit demographic and epidemiological data (reference population - institutional and ICU deaths in the period, ICU bed number and EM reported).

Indicators used: ME/per million population, ME/total institutional deaths, ME/deceased in the ICU, ME/neurocritical deaths, ME/bed (adjusted to occupation). Undiagnosed or reported EMs (EM leak) are detected. The results are returned on a report to institutional authorities and the UCI.

Results: We audited 22/44 public and private institutions during 2016/2021. We analyzed 9,700 deaths in the ICU and audited 1,450 HCs of deceased patients. The EM generation indicators were: EM/deceased in the institution (54%) reached the indicator from 1 to 3%, EM/deceased in the ICU (45%) reached the indicator from 6 to 8% and MO/deceased NC (63%) institutions had a result greater than 15%, ME/Bed adjusted to occupancy). EM leaks were only 107 (7.3% of NC deaths) and 83 (77%) presented adequate medical communication and 24 (23%) were reported EM leaks.

Conclusions: The audit made it possible to identify leaks of brain deaths and to implement corrective/educational measures. The rate of donors increased after the start of this activity that provides information to implement improvement strategies.

Hepatitis B virus Status of Organ Donors in Argentina

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Background & Aims: Argentina is considered an area of a low prevalence of hepatitis B virus (HBV). However, the real prevalence of the disease is unknown. We aimed to study the prevalence of HBV in potential cadaveric donors.

Methods: We performed a cross-sectional study to analyze data from the National Procurement of Transplantation (INCUCAI) in Argentina from 2006 to 2020. We included data from all donors, including tissue only, effective donors (those for whom transplantation was effectively done), and non-effective donors. HBV serologic tests included hepatitis B virus antigen (HBsAg), core antigen-antibody (HBcIgG), anti-HBs. These tests were performed on all donors during the procurement process. HBV status was defined as 1) active HBV: donors with positive HBsAg; 2) Past HBV infection or false positive: isolated positive HBcIgG; 3) Cured infection anti-HBs+/HBcIgG+.

Results: Overall, 16140 deceased donors were denounced. Of these, 8627 (53.5%) were organ donors (7802 [90.4%] were effective) and 7513 (46.5%) were tissue donors. Demographic characteristics were age 42 ± 18 years; male/female ratio was 1.59/1. Overall, the prevalence of HBsAg was 0.37% (n=60) and of isolated HBcIgG+ was 3.6% (n=575). Among organ donors only, 328 (3.8%) presented isolated HBcIgG-positive serology. Of these, 252 (77%) were effective organ donors. Solid-organ transplants performed using isolated HBcIgG+ donors were 220 kidneys, 124 livers, and 27 intrathoracic organs. There was not significant 5-year graft and patient survival difference between HBcIgG+ recipient (kidney transplant 65% and 81%, and for liver 65% and 83% respectively) and general population (kidney transplant 67% (p=0.58) and 92% (p=0.77), and for liver 64% (p=0.73) and 80% (p=0.83), respectively). Anti-HBs data were available in only 4455 donors of which 19% (N=847) were anti-HBs+. In those patients with positive anti-HBs, HBcIgG was positive in 8.3% (n=369), reflecting past HBV infection. Of the remaining 4086 AntiS available, only 11.7% were positive, that is, they were effectively vaccinated. The Patagonia region presented the highest prevalence of HBsAg, especially in the provinces of La Pampa (2.3%), Santa Cruz (2.2%), and Tierra del Fuego (2.1%). The prevalence ratio of HBsAg among donors remained stable during the study period. Isolated HBc IgG-positive donors were only used for organ transplantation, among which 77% (252/328) were effective donors.

Conclusions: The prevalence of HBsAg in deceased donors in Argentina is low. Since the probability of being a donor is random, the prevalence in this population could be close to the real one in the country.
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Cellular Immunity Test and Risk for Cytomegalic Disease in Kidney Transplants

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Introduction: Cytomegalovirus (CMV) is the most common viral infection after kidney transplantation, and is associated with significant morbidity and potential mortality. Taking into account the interaction of the virus with the host’s immune system, recent studies showed that specific CMV CD8+ T lymphocytes play a protective role against viral reactivation. The QuantiFERON®-CMV (QF-CMV) is a technique that monitors interferon (INF-γ) released in response to CMV epitopes. The aim of this study was to evaluate the frequency of CMV-seropositive patients with reactive and non-reactive QF-CMV and their follow up after kidney transplantation, evaluating the frequency of viral replication and treatment necessity.

Methods: We studied 98 renal transplant recipients who had collected the QF-CMV test in the pretransplant moment. CMV seropositive patients were classified according to the QF-CMV result in reactive (≥ 0.2 IU/mL) or non-reactive (< 0.2 IU/mL). After transplant patients were submitted to the center’s usual preemptive treatment, followed-up with qPCR.

Results: 78.6% of the patients were QF-CMV reactive. Time to viremia was shorter in non-reactive QF-CMV patients (68.2 ±15.39 days vs. 135.96 ±28.62 days, p= 0.009). Twenty-nine patients needed CMV treatment, 9 (31%) were non-reactive QF-CMV and 20 (26.3%) were reactive (p= 0.075).

Conclusion: Time to treatment was shorter in non-reactive QF-CMV patients (p=0.004).

248.3

Tuberculosis (TB) Treatment Without Rifampin in Kidney (K) And Kidney-Pancreas (KP) Transplantation (TX)

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Introduction: TB is a diagnostic and therapeutic challenge in K/ KP Tx. Pharmacokinetic interaction between rifampin (RFP) and mTOR/calcineurin inhibitors (CNI) led to use of alternative regimens for TB treatment in this group of patients. Results obtained in TB treatment with RFP-free regimens in K/KP TX patients are presented.

Methods: Retrospective review of confirmed TB cases in K/KP Tx patients. (Jan 2006-Jul 2019), defined by M.tuberculosis positive culture or PCR; o elevated adenosine deaminase (ADA) and/or characteristic histopathology findings with clinical evolution consistent with TB. Cases defined by response to empiric treatment were excluded.

Results: 57 TB cases (50 in 2297adults with KTx (2.2%)/7 in 364 KPTx (1.92%). Two were postmortem diagnosis (excluded from analysis). “De novo” Treatment with RFP-free regimens: 30 patients (pts) (25 KTx, 5 KPTx). Mean age: 49.24 ±11.50 years. Induction immunosuppression (IS): 22 pts. Maintenance IS: tacrolimus-mycofenolate (MF)-steroids (E) in 13 (43%), sirolimus-MF-E in 6 (20%), Other IS regimens: 11(36%). Belatacept in 4 patients. (13%). 22 pts without rejections (R) prior to TB, 8 pts with R: Rejection rate prior to TB 0.15 episodes/year/patient. TB onset after TX: Median 28 (range 2.4- 242.3) months. Late onset (> 6 months): 24 cases (80%). TB: pulmonary = 13 (43%); Disseminated = 7 (23%) Extrapulmonary = 10 (33%). All patients were treated with isoniazid (IHN), ethambutol (EMB), levofloxacm (L), 12 patientes also received pyrazinamide (PZN) during the first 2 months. 27 (90%) patients completed treatment with IHN-EMB-L x 6 months (1), 9 months (3) o 12 months (23). In these patients, graft function had no change (mean initial creatinine 1.5 mg%, mean creatinine at end of treatment 1.5 mg%, p=NS). One patient returned to dialysis at 4th month of treatment, and completed with IHN-RFP. 2 (7%) patients died while on treatment. Among the 28 patients who completed treatment, median (range) follow-up was 32 (8-150) months. No TB relapses were observed.

Conclusions: Rifampin-free TB treatment in K/KP Tx was safe and effective. Mortality was less than observed in series with a larger number of patients treated with rifampin. The use of RFP-free regimens also avoided cumbersome pharmacokinetic interactions with CNI/mTOR, with excellent results in grafts function.
Abstracts

248.4

Oral Antibiotics for Treatment of Gram Negative Bacteremia in Solid Organ Transplant Recipients: A Retrospective Observational Study

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Introduction: Treatment of gram-negative bloodstream infection (GNBI) with oral rather than intravenous (IV) antimicrobial agents can reduce length of stay, line associated complications and improve overall patient satisfaction. Data in immunocompetent subjects supports use of highly bioavailable oral agents for treatment of uncomplicated GNBI, however there is minimal literature regarding the safety and efficacy of this practice in solid organ transplant recipients (SOTR). We aimed to assess the safety and efficacy of oral for treatment of uncomplicated GNBI in SOTR.

Methods: We performed a retrospective observational study and identified all SOTR with GNBI within the Massachusetts General and Brigham and Women’s Hospital systems from 2016-2021. We then identified patients who were transitioned from intravenous to oral agents to complete their treatment. To be considered eligible for analysis, patients had to have adequate source control and could not have evidence of a complicated infection (e.g endocarditis, osteomyelitis, undrained abscess) that would inherently require a prolonged treatment course. We recorded patient demographics, type of and time from transplant, comorbidities and Charlson comorbidity score, PITT bacteremia score, immunosuppressive regimen, and eGFR at time of transition to an oral agent. We noted the source of infection, infecting organism, antimicrobial agents used and duration of oral and IV therapy. Primary endpoints were mortality, recurrence of bacteremia and re-initiation of IV antibiotics for the same underlying infectious process within 30 days of treatment completion. Secondary endpoints included length of stay, development of C difficile infection, treatment associated complications, and need for further oral antibiotics directed at the initial infectious process. We are collecting further data on a control population.

Results: 119 GNBI's from 106 patients met inclusion criteria. The most common transplant type was kidney (n=83). E. coli was the most frequently identified organism (n=50). The most common source was urinary (n=71) and the most commonly used oral antimicrobial was ciprofloxacin (n=80). Median duration of oral therapy was 11 days (range 3-30 days). Median time from transplant was 3 years (range 1 week – 42 years). Zero patients died within 30 days of treatment completion. Secondary endpoints included length of stay, development of C difficile infection, treatment associated complications, and need for further oral antibiotics directed at the initial infectious process. We are collecting further data on a control population.

Conclusions: Conversion from IV to oral therapy with highly bioavailable antimicrobials is safe and effective for treatment of GNBI in SOTR. Randomized controlled trials are needed to confirm these findings.

Table 1: Clinical Characteristics of Solid Organ Transplant Recipients Treated with Oral Antimicrobials

<table>
<thead>
<tr>
<th>Organ Transplant Type</th>
<th>Total Patients (n)</th>
<th>Acute Kidney</th>
<th>Heart</th>
<th>Lung</th>
<th>Small Bowel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>106</td>
<td>83 (79%)</td>
<td>15 (15%)</td>
<td>5 (5%)</td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>

Table 2: Treatment and Outcomes of Solid Organ Transplant Recipients Treated with Oral Antimicrobials

<table>
<thead>
<tr>
<th>Oral Antibiotic</th>
<th>Total Antibiotic Duration (days)a</th>
<th>Length of Stay (days)</th>
<th>IV Duration (days)b</th>
<th>Oral Duration (days)</th>
<th>Total Patients (n)</th>
<th>Other Treatment Related Complicationsc</th>
<th>Mortalityd</th>
<th>Bacteremia Recurrenced</th>
<th>Transition Back to IV Therapye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>16.2</td>
<td>6.9</td>
<td>4.8</td>
<td>1.11</td>
<td>106</td>
<td>3 events (%)</td>
<td>0 patients (0%)</td>
<td>2 patients (2%)</td>
<td>6 patients (5%)</td>
</tr>
</tbody>
</table>

aDuration of IV therapy prior to transition to an oral agent.
bWithin 30 days of completion of antibiotic treatment course.
cWithin 30 days of completion of antibiotic treatment course.
dWithin 30 days of completion of antibiotic treatment course.
eTransition back to IV therapy directed at the initial underlying infectious process. Includes the 2 patients with bacteremia recurrence and 4 additional patients without bacteremia recurrence.
248.5

Development of Serological Tools for Diagnosis of Human Herpesvirus 8 Infection and Their Application to Estimate Antibody Prevalence in English Blood and Organ Donor Populations

Anna Godi1, Yara Hajarah1,2, Stephen Dicks1,2, Keerthana Jegatheesan1,2, Samreen Ijaz1, Ines Ushiro-Lumb1,2.
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Introduction: Human Herpesvirus 8 (HHV-8), also known as Kaposi sarcoma-associated herpes virus, is aetiologically associated with all forms of Kaposi's Sarcoma (KS), including transplant-related, as well as rare neoplastic conditions such as primary effusion lymphomas and multicentric Castleman disease. Solid organ transplant recipients have a much higher risk of KS compared to the general population and the role of serological screening in this setting has been long debated; there is currently no standard method of screening for HHV-8 infection and serology has been largely used for sero-epidemiological purposes. The latent nature of the virus makes determination of HHV-8 infection status complex and investigations may lead to inaccuracies.

Methods: To fulfil the critical gaps in the diagnosis of asymptomatic virus infection, a combination of serological tools for the detection of antibody to both HHV-8 lytic and latent antigens have been developed and compared with the commercial lytic antigen-based immunofluorescence assay (IFA, Scimedx Corp), which is commonly used in Europe for the detection of antibodies to HHV-8. The developed assays include an in-house latent IFA assay that utilises latently infected PEL cells as well as two Double Antigen Binding Assays (DABAs) which utilise major HHV-8 antigens; ORF73 and K8.1 (latent and lytic proteins, respectively).

Results: Initial data gained from the testing of samples from identified patients with ongoing HHV-8 disease indicate a good concordance between both latent and lytic antibody assays. Studies are underway to determine the performance of these assays for the identification of asymptomatic infection and are being applied to establish the prevalence of HHV-8 antibodies in donor populations.

Conclusion: HHV-8 has a complex serological profile and the availability of tools based on a range of formats which target multiple proteins will better inform on seroprevalence rates both at a population level and within specific at-risk groups.

248.6

BK Virus Infection in Kidney Transplant Patients at Hospital De Clinicas - Paraguay

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Introduction: The BK virus, belonging to the polyomavirus family, was first described in 1971 in a kidney transplant with ureteral stenosis, which eliminated cells with atypical nuclear morphology in the urine, and the name of the virus was established by the initials of the patient. Primary BK virus infection usually occurs in the first decade of life. After it, the virus colonizes the urinary tract and remains dormant in kidney cells. When immunity declines, the virus begins to replicate in the epithelial cells of the kidney, ureter, and bladder. In kidney transplantation, it can lead to the development of nephropathy and graft loss.

Materials and Methods: Observational, descriptive cross-sectional study. A review of a population of kidney transplant patients from living and cadaveric donors, over 18 years of age was made. 66 patients from whom quantitative polyomavirus BK-DNA viral load in plasma and urine was requested for a clinical indication from 2019 to 2022 were selected. Clinical, analytical, demographic, gender, type of transplant, and record of results variables were collected.

Results: Of 66 patients who were asked to have quantitative BK-DNA polyomavirus in plasma and urine, 23 patients tested positive for BK-DNA virus in plasma or urine, 82% were male, 56% were living donor patients, the debut mean VBK was at 48+/- 29.36 months. Of these 23 patients, 26% had a positive result only in urine and the rest in plasma and urine, 26% had impaired kidney function and the rest had stable kidney function from diagnosis to the present time, 2 patients had acute humoral rejection at the same time and one recurrence of his underlying glomerular disease. Of the patients who maintained stable renal function values, all had decreased immunosuppression, 14 patients were switched from tacrolimus to cyclosporine and 1 to mtor.

Conclusion: Early diagnosis of the infection alerts us to decreased immunosuppression, however, when concomitant rejection is associated, management can be more complicated. It is important to establish a screening protocol in transplant centers and to suspect this infection if there are symptoms or deterioration of renal function.
Cat Scratch Related Acute Glomerulonephritis in a Kidney Transplant Recipient

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Objective: Bartonella Henselae (BH) infection is known to lead to life-threatening complications, especially amongst immunocompromised kidney transplant patients. We report a case of post-infectious glomerulonephritis in a kidney transplant recipient secondary to BH.

Methods: A 42-year old man who underwent a deceased donor kidney transplant with a baseline creatinine of 2 mg/dL, on tacrolimus and mycophenolate based immunosuppression regimen with early steroid withdrawal, presented 4 months post-transplant with AKI, fever and pancytopenia. Labs are as shown in Table 1.

Results: Work up was notable for bartonella henselae bacteremia. He underwent an allograft biopsy that demonstrated post-infectious glomerulonephritis (GN); Mycophenolate was discontinued and treatment was started with rifabutin and doxycycline. AKI initially improved, but later worsened and a second biopsy was performed, which revealed a pattern of diffuse supplicative proliferative GN (Fig. 1) with focal crescents (Fig. 2). Electron microscopy revealed sub-endothelial and sub-epithelial electrondense immune deposits. The immune deposits were predominantly IgA, IgM and C3, and negative for IgG. He was started on IV steroid pulse and initiated on dialysis for worsening volume overload. Four weeks after discharge a follow-up biopsy was performed as the patient remained on dialysis. The biopsy showed a focal proliferative GN with more segmental intra-membranous immune deposits and rare sub-epithelial humps, a pattern consistent with resolving post-infectious GN. Soon after he came off dialysis with resolving acute kidney injury.

Conclusions: There is limited literature published on infection related glomerulonephritis in transplant recipients with Bartonella. The few documented cases with Bartonella post-transplant have been seen in association with native valve endocarditis. Our patient had no vegetation on Echocardiogram. Given the severity of disease on pathology, with crescents, pulse dose steroids likely helped decrease inflammation. This is a unique case of Bartonella induced infection related glomerulonephritis that led to AKI requiring dialysis with resolution following treatment with antibiotics, immunosuppression reduction and steroid therapy.

<table>
<thead>
<tr>
<th>Admission Labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
</tr>
<tr>
<td>Platelets</td>
</tr>
<tr>
<td>Creatinine</td>
</tr>
<tr>
<td>Urine Protein</td>
</tr>
<tr>
<td>Urine RBC / WBC</td>
</tr>
<tr>
<td>B Henselae IgG</td>
</tr>
<tr>
<td>B Henselae IgM</td>
</tr>
<tr>
<td>C3/C4 Complement</td>
</tr>
</tbody>
</table>
248.8

**Mycobacterium tuberculosis Colitis and Cytomegalovirus in A Renal Transplant Recipient: An Infrequent Association**

Paola P García1,2, Kateir Contreras1,2, Paola Panra1,2, Oscar Lucero2, Natalia Sánchez2*

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**Introduction:** Chronic diarrhea, infectious or inflammatory, is a frequent cause of consultation in transplant recipients. Immunosuppressors are the most common reason, but microorganisms like cytomegalovirus (CMV), clostridium difficile, campylobacter, are often reported. Tuberculosis can occur, but it has a low prevalence, described between 0.3 and 1.7%.

**Method:** We described a 32-year woman with a history of membranoproliferative glomerulonephritis, recipient of a deceased-donor kidney transplant 12 years ago. She received basiliximab and steroids as induction therapy and maintenance with tacrolimus, mycophenolate and deflazacort. She consulted with a 7-day history of liquid diarrhea, no blood, nor mucus with abdominal pain, nausea, and fever up to 39°C. She manifested a 10kg loss of weight in a 6-month period with no other symptoms. Upon admission, she had tachycardia, mild abdominal pain in left flank. Blood workup showed normal leukocytes and platelets, absolute lymphocyte count of 0.8x10³ / L, hemoglobin 8.9g/dL, creatinine 1.51mg/dL, high C-reactive protein, and low level of albumin. Low iron, TSAT, and ferritin level. Normal folic acid and vitamin B12. Coproscopic showed blood, no leukocytes. Blood cultures, molecular panel identification of multiple gastroenterology pathogens (filmarray), VIH, viral load with transcriptase-polymerase-chain-reaction (PCR) in blood for CMV were negative. Chest radiography was normal. Contrast abdominal tomography showed thickening and enhancement of the walls of the cecum, hepatic flexure, ileocecal valve and distal ileum. In ascending colon, a 4cm decreased of the lumen was seen. Multiple round nodes smaller than 10mm after contrast were observed. Total colonoscopy showed colitis in transverse and left colon with 80% stenosis of the lumen.

Biopsy documented active chronic colitis with a marked ulcerative component. No microorganisms, dysplasia or malignancy were observed. Real time-PCR was processed for CMV in colonic tissue and PCR for mycobacterium tuberculosis (MT) both reported positive. Co-infection with intestinal CMV and MT was diagnosed. She was treated with valganciclovir for 4 weeks and pyridoxine. During treatment, presented elevated transaminases and conjugate with isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E) and pyridoxine. Moxifloxacin, R and Z were continued for 9 months. The patient had resolution of the diarrhea, recovery of weight, anemia and renal function.

**Conclusion:** CMV is a common etiologic agent in kidney transplant recipients with diarrhea, co-infection with other microorganisms, such as, MT can worsen the clinical course and without treatment can lead to death. Having a high index of suspicion is essential. A rigorous diagnostic approach is necessary and performing PCR on tissue can contribute to allow early diagnosis and timely treatment.

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248.9

**COVID 19 Survival Among Lung Transplant Recipients: A Single Center Study From Hospital Universitario Fundación Favaloro/Buenos Aires**

Juan Calderón1,2, Juana Rosalia Ahumada1,2, Teresa Ibañez1, Viviana Nazzo1, Nadya Bejarano2, Jorge Osvaldo Caneva2, Silvia Moscoloni1, Liliana Martínez1, Jorge Vicente2, Mariano Candioti1, Juan Manuel Ossés1,2, Alejandro Bertolotti1,2,3*

1Trasplante Intratorácico, Hospital Universitario Fundación Favaloro, Caba, Argentina; 2Servicio de Neumología, Hospital Universitario Fundación Favaloro, Caba, Argentina; 3Servicio de Kinesiología y Rehabilitación, Hospital Universitario Fundación Favaloro, Caba, Argentina.

**Introduction:** Patients after lung transplantation (LTx) are at risk for life-threatening COVID 19 because of chronic immunosuppression. Although several publications in this patient population appeared, scarce data is available in South America.

**Method:** Observational, retrospective study from a high-volume lung transplant center in Buenos Aires, Argentina. All LTx recipients with COVID-19 diagnosed from 3 March 2020 to 30 March 2022 were included. We analyzed demographics, clinical features, therapeutic management, immunosuppression, previous COVID 19 vaccination, and survival. Data are shown as median and range or as absolute and relative frequencies as appropriate. Categorical variables were compared using Chi square, and continuous variables were compared using Mann-Whitney U-test. The Kaplan-Meier test was used for statistical analysis and p value <0.05 was statistically significant.

**Results:** 44 patients were diagnosed, mainly using RT PCR SARS CoV2 test (90%). Most were male (66%), 77% underwent bilateral LTX and 2% of heart-lung transplantation; with a diagnosis of Cystic Fibrosis in 46% of cases followed by ILD (20%) and COPD (11%). Mean age at time of diagnosis were 42.9 years old (CI 95% 39.1-46.9), with a mean time (months) after LTx of 58.11 (CI 95% 43.4 – 72.8), and BMI of 24.17 (CI 95% 22.5 – 22.8). Most of LTx recipients were not vaccinated (n=23, 52%) at the time of diagnosis, and 13.6% of infections were in 2020 and 45.4% in 2021. Half of patient (48%) developed pneumonia; 32% received steroids (other than traditional immunosuppression) and antibiotics, and 5% received plasma. 25 patients (57%) were admitted to hospital of which 48% (12/25) were admitted at ICU (66.7% in mechanical ventilation). 83% of not vaccinated were admitted to ICU compared versus 17% of vaccinated patients (p=0.04). In general, death related to COVID 19 were 16% (N=7), all in not vaccinated group (p=0.04) with a median of 16 days of survival (Fig. 1). No differences were found by age, BMI and time of infection.

**Conclusion:** In our center, LTx recipients develop the entire spectrum of COVID-19. There has been a lot of discussion whether immunosuppressive treatment needs to be continued, lowered or even temporarily stopped in case of a COVID-19 infection. Immunosuppression was not discontinued in most patients (tacrolimus, methylprednisone, and mycophenolate), except in patients receiving mechanical ventilation (hydrocortisone). The main factor related to death was no vaccination. Interestingly, less than quarter of infectious occurred in 2020 likely related to strict lockdown in our country.
COVID-19 Infections in Pediatric Renal Transplant Recipients

Aysun Çalışk Yılmaz1, Esra Baskın1, Kaan Guilleroglu1, Aydinçan Akdur1, Gökhan Moray2, Mehmet Haberal2

1Department of Pediatric Nephrology, Baskent University, Ankara, Turkey; 2Department of General Surgery, Division of Transplantation, Baskent University, Ankara, Turkey.

Introduction: The most of research to date indicates that children who have received a renal transplant are not at elevated risk of COVID-19 infection and generally have a mild illness course. Children are recognized as having a lower risk of severe COVID-19 infection than adults, although the most of pediatric renal transplant recipients had mild symptoms, severe illness and death have been reported in a small proportion of patients.

Materials and Methods: Between March 2020 and October 2021, COVID-19 was researched in kidney transplant recipients under the age of 19 who were followed at Başkent University Transplantation Center. We documented the clinical characteristics and prognosis of pediatric kidney transplant recipients with COVID-19 disease.

Results: We present 26 cases of COVID-19 infection from 215 pediatric patients with kidney transplantation. The average age of the patients was 14.2 (range 4-19), with 11 of them were female. The mean follow-up time after transplantation was 66.8 (range 6-148) months. In 16 patients (61.5%), fever was the most frequent symptom. Seventeen patients (65%) had mild respiratory symptoms such as cough, chest pain and loss of smell. Our 5 patients (21%) needed hospitalization. Four of them also developed acute kidney injury. One of these patients was hospitalized with a diagnosis of COVID-19 infection one week after being treated with IVIG and rituximab for acute antibody-mediated rejection. That patient developed significant lung disease and multi-organ failure. The second patient was a 5-year-old male who was admitted to the hospital due to diarrhea and required fluid and electrolyte replacement. Other hospitalized patients developed pneumonia but did not require intubation and recovered fully with antibiotic, antiviral and supportive therapy. Most of our patients (80.7%) had minor symptoms and recovered completely after receiving supportive treatment.

Conclusion: According to our experience, COVID-19 is generally overcome with mild symptoms in pediatric renal transplant patients. Due to new vaccines and new virus strains, the clinical picture may alter in coming years.

Torque Teno virus Load as Functional Marker of Immune Function in Solid Organ Transplantation: A Systematic Review And Meta-Analysis

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Background: Balancing immunosuppression to prevent rejection and infection in solid organ transplant recipients (SOTx) remains a challenge. Torque teno virus (TTV), a commensal non-pathogenic virus, has been proposed as functional marker of immunity: higher loads reflect over-immunosuppression, while lower loads reflect under-immunosuppression. Here we present a systematic review and meta-analysis of the current literature and provide evidence on the association between TTV load and infection and rejection in SOTx recipients.

Methods: A systematic literature search strategy, deposited in PROSPERO, resulted in 548 records. After screening, 23 original and peer-reviewed articles were included in qualitative assessment, investigating the association between TTV load, and either infection or rejection in SOTx. The Quality in Prognosis Studies (QUIPS) tool was used to assess the risk of bias. Meta-analysis was performed on studies with similar outcomes measures and exposure using a joint modelling strategy.

Results: 23 studies were included, most involved retrospective cohorts in which the TTV load was measured within 1-2 years post-transplantation, once or longitudinally. Defined outcomes differed between studies, and included viral (CMV, BK, respiratory), bacterial, and fungal infections. Rejection outcomes included rejection treatment, with or without biopsy confirmation. QUIPS assessment showed varying risks of bias between studies. Twelve out of 17 studies reported an association between high TTV loads and infection (71%), and 13 out of 15 an inverse association between low TTV loads and rejection (87%). Meta-analysis showed an increased risk of infection (OR: 1.16, CI 1.04-1.30; HR: 1.05, CI 0.97-1.14) and decreased risk of rejection (OR: 0.90, CI 0.87-0.94, HR: 0.74, CI 0.71-0.76) per 1 log TTV load increase.

Conclusions: Systematic review of the current literature shows an association between TTV load and each outcome in most studies, and this association is supported by our meta-analysis. However, concerns on study quality and the risk of publication bias warrants careful interpretation. Externally validated prediction models using TTV load remain to be built, as these will offer individualized diagnostic or prognostic value to predict infection and rejection in SOTx recipients.
248.12

Critically Important Outcomes for Infection in Trials in Kidney Transplantation: An International Survey of Patients, Caregivers and Health Professionals

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1Department of Medicine, Division of Infectious Disease, University of Miami Miller School of Medicine, Miami, FL, United States; 2Miami Transplant Institute, Jackson Health System, Miami, FL, United States; 3Department of Medicine, Division of Nephrology, University of Miami Miller School of Medicine, Miami, FL, United States; 4Department of Medicine, Division of Hepatology, University of Miami Miller School of Medicine, Miami, FL, United States; 5Department of Pathology, University of Miami Miller School of Medicine, Miami, FL, United States; 6Department of Medicine, Division of Pulmonology, University of Miami Miller School of Medicine, Miami, FL, United States; 7Department of Medicine, Division of Nephrology, University of Miami Miller School of Medicine, Miami, FL, United States.

Introduction: Solid organ transplant (SOT) recipients are at high risk for severe disease with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Emerging variants of concern have disproportionately affected this population. Data on severity and outcomes with the Omicron variant in SOT recipients is limited.

Methods: Single-center, retrospective cohort study of SOT recipients diagnosed with SARS-CoV-2 infection from December 18, 2021, to January 18, 2022, when prevalence of the Omicron variant was more than 95% in the community. Univariate and multivariate logistic regression analysis was performed to identify risk factors for hospital admission.

Results: We identified 166 SOT patients – 125 (75.3%) kidney, 27 (16.2%) liver, 10 (6.0%) lung, 8 (4.8%) heart, 9 (5.4%) combined transplants [Table 1]. SARS-CoV-2 vaccine series was completed in 59 (35.5%) recipients. Ninety-nine (59.6%) and 13 (7.8%) recipients received casirivimab/ imdevimab and sotrovimab, respectively [Table 2]. Fifty-one (31.6%) recipients required hospital admission, of which 17 (33.3%) required intensive care unit level of care. Anti-metabolite agents were decreased or stopped in 74/125 (59.2%) patients. Median time of follow up was 14 days (IQR, 9-18), with mortality reported in 2 (1.2%) patients. Kidney function was compared among patients before, at time of, and 1-month post-diagnosis of COVID-19. Median creatinine was 1.3mg/dL (range 0.5–9.4), 1.3mg/dL (range 0.6–10.7) and 1.27mg/dL (range 0.6–10.4) respectively. Creatinine was statistically significantly increased after COVID-19 diagnosis (p<0.001), however 1-month post-transplant, there was no statistical difference when compared to prior to transplant (p=0.31). Risk factors identified for hospital admission were African American race (p<0.001, Odds ratio [OR] 4.00, 95% Confidence Interval [CI] 1.84–8.70), history of coronary artery disease (p=0.031, OR 3.50, 95% CI 1.12–10.87), and maintenance immunosuppression with corticosteroids (p=0.048, OR 2.00, 95% CI 1.01&ndash;4.00).

Conclusion: Similar to the general population, we found low mortality and high hospital admission rate in SOT recipients with omicron variant infection. Further studies to investigate the efficacy of newer treatments are necessary, even as outcomes continue to improve.
Impact of COVID-19 Infection on Children and Adolescents After Liver Transplantation in a Latin American Reference Center

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Background & Aims: Published studies suggest that children (<18 years) infected with COVID-19 are less likely to progress to the severe form of disease when compared to adults, however, scarce data are available on morbidity and mortality in immunocompromised children and adolescents. The aim of this study was to evaluate the outcomes of Pediatric Liver Transplant Recipients (PLTR) who were infected with COVID-19.

Methods: Prospective longitudinal cohort study. Between 1st March 2020 and 31st October 2021 clinical, laboratory and evolution data from PLTR (<18 years) were collected in person or by remote telemedicine, who tested positive for COVID-19, for presenting symptoms suggestive of COVID-19 infection or positive epidemiological screening or for presenting positive in laboratory screening before procedure – incidental positive.

Results: A total of 74 PLTR were diagnosed with COVID-19. The mean age was 8.2 years (SD 4.49) and 51.4% were girls. The prevalent indication for liver transplantation (LT) was biliary atresia 48 (64.8%) and in 69 (93.2%) patients LT was performed with a living donor. The mean time between LT and COVID-19 infection was 60 months (SD 57.7) and 5 (6.7%) patients became infected up to 3 months after LT, 2 in the early postoperative period. Most patients developed mild symptoms (66%) such as fever (25%), cough (20.2%) and runny nose (20.2%). Hospitalization of outpatients was necessary in 6 children (8.1%), all in hospital ward for suspected sepsis (1), respiratory distress (2), periorbital cellulitis requiring parenteral antibiotics (1), vomiting (1) and gum-stomatitis (1) both requiring hydroelectrolic replacement. Only 1 child, previously admitted to hospital ward, required transfer to the ICU for respiratory support. The main comorbidities were atopic dermatitis in 5 patients (6.7%), asthma in 4 (5.4%), heart disease, neurological diseases and food allergy in 3(4%), none of which was related to the severity of presentation of COVID-19 infection. Baseline immunosuppression was based on tacrolimus, being associated with prednisone and mycophenolate in 28% and 13.7% respectively. Change in immunosuppression was required with mycophenolate discontinuation in 3 (4%) and a decrease tacrolimus level in 1 patient. Most patients had a good recovery, and only 1 child developed Multisystem Inflammatory Syndrome associated with COVID-19 infection. No child died in this study cohort.

Conclusion: In pediatric population LT and immunosuppression cannot be considered independently as factors associated with the risk of severity and death due to COVID-19.

Variable | All Patients | N (%) | N (%) |
--- | --- | --- | --- |
**Demographics** | | | |
Age, median (IQR) | 57 (40 - 41) | | |
Gender, Male | 95 (38.4%) | | |
Race, White | 120 (75.9%) | | |
Other, Hispanic | 99 (59.0%) | | |
**Comorbidities** | | | |
Hypoension | 120 (77.7%) | | |
Diabetes Mellitus | 54 (32.3%) | | |
Chronic kidney disease | 14 (8.4%) | | |
Coronary artery disease | 15 (9.9%) | | |
COPD | 10 (6.5%) | | |
HIV | 3 (1.8%) | | |
**Transplantation** | | | |
Kidney | 125 (79.3%) | | |
Liver | 27 (16.2%) | | |
Heart | 8 (4.9%) | | |
Long | 10 (6.0%) | | |
**Procced** | | | |
Plaque | 7 (4.2%) | | |
Multiviewed | 2 (1.2%) | | |
**Maintenance Immunosuppression** | | | |
Tacrolimus | 140 (89.7%) | | |
Mycophenolate mofetil | 25 (12.9%) | | |
Mycophenolate mofetil | 125 (79.3%) | | |
Belatacept | 7 (4.2%) | | |
Sirolimus | 83 (53.2%) | | |
**Time from transplant to diagnosis (months), median (range)** | 27 (0.6 - 262) | | |
**Days of symptoms presentation, median (IQR)** | 3 (2-5) | | |
**Prior history of COVID-19** | | | |
Yes | 11 (15.0%) | | |
No | 63 (85.0%) | | |
**Vaccination status** | | | |
Complanted primary series | 50 (35.5%) | | |
Receved 2 vaccine doses | 61 (37.9%) | | |
Receved 1 vaccine dose | 7 (4.2%) | | |
Unknown | 37 (23.1%) | | |
**COVID-19 Antibody data** | | | |
IgG detected | 95 (37.2%) | | |
IgG negative | 60 (95) | (94.4%) | |

Footnotes: *: Data presented as absolute number (percentage), unless specified otherwise.
**: Individual percentage values are rounded and might not total 100%.
Follow-up Status After Recovery From COVID-19 Infection in Kidney Transplant Recipients: A Single Center Experience From India Across Various Pandemic Waves

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Introduction: There is dearth of knowledge for the follow-up studies with regards to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in kidney transplant recipients (KTR). We have previously reported first such report of a small cohort. Herein we analyze long-term outcome of COVID-19 infection in KTR across different pandemic waves including delta and omicron wave.

Methods: We conducted this retrospective, single center cohort study of hospitalized (n = 367) and non-hospitalized KTR (n = 197) for a median (range) follow-up of 14 (1-20) months who recovered from SARS-CoV-2 during May 2020 to Jan 2022. All confirmed RT-PCR cases with at least 3-month follow-up were included. The outcomes measured were persistent symptoms post-discharge; EuroQol visual analogue score (EQ-VAS); EuroQol 5-dimension score (EQ-5D-5L) score and modified medical research dyspnea score (mMRC) at discharge, 3 months and last follow-up. Other outcomes were graft outcome and postulated COVID-19 sequelae.

Results: The median (range) age of the cohort was 44 (15-71) years and COVID-19 severity ranged from asymptomatic (14%), mild (40%), moderate (36%) to severe (10%). The most common persistent symptom was generalized which significantly decreased in the follow-up (n = 110 vs. 53 vs. 11); p-value = 0.0001) at discharge, 3-month, and last follow-up respectively. Decrement in the mean (standard deviation) EQ-VAS score from baseline was also improved (36 [13] vs. 17 [12.5] vs. 8 [12.0]; p-value < 0.0001). There was statistically significant improvement in all EQ-5D-5L scores in follow-up. There was no deterioration in mMRC scores during the follow-up Moderate-severe cases had significantly poorer overall scores initially, but there was no difference at long-term follow-up. 27 of 30 graft losses reported had baseline chronic graft dysfunction at baseline. There were no unexplained deaths, pulmonary fibrosis, cardiovascular event or cerebrovascular event.

Conclusion: We report the largest cohort of Indian transplant recipients with COVID-19 at longest follow-up. Improvement in quality of life and no postulated COVID-19 sequelae ensures that no residual abnormality exist in post-COVID-19 KTR.

COVID-19 Outcomes After Widespread Vaccine Availability in Kidney Transplant Recipients

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Introduction: In 2020, 16% of deaths among kidney transplant (KT) recipients in the United States were due to COVID-19, and KT recipients remain at high risk for severe complications. The impact of vaccination on COVID-19 outcomes in KT recipients remains incompletely described. Our aim was to review the outcomes of our center’s KT recipients who contracted COVID-19 after the availability of vaccines.

Methods: We retrospectively reviewed all KT recipients at Wake Forest Baptist Medical Center (Winston-Salem, North Carolina, USA) performed between 2016 and 2020 with a known laboratory-proven diagnosis of COVID-19 from 03/2021 through 02/2022. Demographic, vaccination, hospitalization and outcome information were reviewed for these patients.

Results: 1017 patients underwent kidney transplantation at our center between 2016-2020, including 11 patients who died of COVID-19 complications prior to March 2021. We identified 58 patients (5.7%) with laboratory-proven COVID-19 between March 2021 and February 2022. Of these patients, 33 (56.9%) were men and 25 (43.1%) were women. The average age at COVID-19 diagnosis was 53 years (44.8%) to severe (10.3%) were Asian, Native American, or other groups. 5 (8.6%) identified as Hispanic/Latino. Compared with the total KT population for the study period, COVID-19 was diagnosed in 33/539 (6.1%) of men, 25/478 (5.2%) of women, 24/518 (4.6%) of White patients, 27/414 (6.5%) of Black patients, 5/50 (10%) of Hispanic/Latino patients, and 7/85 (8.2%) of other groups. Of the patients with COVID-19, 42/58 (72.4%) had received at least one vaccine dose. 8 patients were infected with COVID-19 between 3/1/21 and 6/30/21, 16 during the Delta variant from 7/1/21 to 11/15/21, and 34 during the Omicron variant from 11/16/21 to 3/1/2022. Venous thromboembolism occurred in 7/58 patients (12.1%), acute kidney injury in 26/58 (44.8%), and transplant rejection in 1/58 (1.7%). Overall, 31/58 patients required hospitalization (53.4%), 10/58 required ICU admission (17.2%), and 6/58 died (10.3%). Of these deaths, 5 occurred in the hospital, while 1 occurred at home shortly after hospital discharge.

Conclusion: In this single-center analysis, we identified a high risk for severe complications of COVID-19 in KT recipients, even with vaccination. Overall, COVID-19 mortality was lower following vaccine availability in our center compared with the pre-vaccine period. Our present cohort size is almost certainly an underestimate, but there was a marked increase in diagnosed cases during the Omicron wave compared with earlier variants. A majority of identified patients required hospitalization, with a high risk for death. Infection appeared more common in minority groups and in men. Continued precautions will be necessary to protect KT recipients during the ongoing pandemic.
COVID-19 Infection After Pancreas Transplantation
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Introduction: Transplant recipients are at elevated risk of COVID-19 infections. Pancreas transplant recipients (PTR) are an understudied group. We wanted to determine COVID-19 vaccination, infection, and breakthrough infection rates in PTR.

Materials and Methods: We performed a retrospective review of 176 PTR performed between 1/1/2014-2/1/2022. Summary data are presented as mean+/−standard deviation. Bivariate comparisons to evaluate characteristics associated with outcomes were performed using Fisher’s exact test.

Results and Discussion: The mean age at transplant was 45.3+/−9.1 years, and the mean current BMI 27.9+/−5.6. There were 96 (53%) males, 90 (50.3%) were white, 68 (38%) black, 8 (4.5%) Asian, and 10 (5.6%) others. The majority were SPK recipients (76%). During a mean of 1228+/−687 days of follow-up, there were 12 organ failures (8 P 2 K, 2 SPK). Of patients who developed a COVID infection, only 2 (3%) patients died (with functioning grafts) from COVID infection. Both were fully vaccinated with 2 and 3 doses, respectively. A third patient died from unrelated causes.

Conclusion: In this cohort of 176 PTR, the infection rates in PTR were 33% (CI95% 25.2-42.2) and 8 (4.5%) deaths (CI95% 1.4-17.5). The majority were SPK recipients (76%). The infection rates in PTR were 33% (CI95% 25.2-42.2) and 8 (4.5%) deaths (CI95% 1.4-17.5). The majority were SPK recipients (76%).

Fast Decrease of Humoral Response Against SARS-CoV-2 in A Kidney Transplant Cohort
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Introduction: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread from Wuhan, China since December 2019 and caused a large ongoing pandemic disease with high morbimortality. In Brazil the disease caused more than 22 million cases and 600 thousand of COVID-19 related deaths in the country at the end of the second wave. Immunocompromised hosts such as kidney transplant recipients (KTR) were expected to have higher risk for severe disease and death due to their compromised T cell responses. There are few studies evaluating the immunological response and antibody dynamics to vaccine and natural infection stimulus in transplant recipients. The present study aims to estimate SARS-CoV-2 seroprevalence in KTR assisted at tertiary university hospital of São Paulo-Brazile through a longitudinal design.

Methods: This is a prospective cohort of outpatient KTR based on four consecutive serological surveys plus clinical and epidemiological questionnaires. We present here the preliminary results from two completed surveys (performed from April to June-2021 and from Aug to Sept-2021, respectively). Presence of antibodies against SARS-CoV-2 was assessed using an electro-chemiluminescence immunoassay for qualitative detection of antibodies to SARS-CoV-2 nucleocapsid, the Elecsys Anti-SARS-CoV-2 from Roche (cut off index ≥ 1.0 = reactive, sensitivity of 99.5% and specificity of 99.8%). We considered effective vaccine doses if they have been administered at least 14 days before blood sample collection. We characterized three groups according to the number of effective vaccine doses administered between the first and second surveys: Group OD, those who did not receive any dose; Group 1D, those who received 01 dose and Group 2D, those who received 02 dose between surveys.

Results: We recruited 170 participants; positivity rates in the first and second surveys were 20.1% (C195% 14.2-26) and 23.2% (C195%15.4-30.9). Only 95 (55%) participants completed both surveys with a median of 105 days (range 54-154) between surveys. Loss of follow-up were due to seven deaths related to COVID-19, one graft loss and ninety did not collect blood samples in time for the second survey. Confirmed COVID-19 was detected in 29 cases previously to survey 1 and in 6 cases between surveys 1 and 2. Excluding confirmed COVID-19 participants between surveys 1 and 2, the seroprevalence analysis showed an increase in seroprevalence rates as expected for Groups 1D and 2D but revealed an important decrease on the seroprevalence rates for Group OD – from 13.6% (C195% 2.9-35) to 9.1% (C195% 1.1-29) between surveys.

Conclusion: In this cohort of outpatient KTR of a tertiary hospital in São Paulo city, we highlight the decrease of seroprevalence rates between the surveys among those who were not exposed to any stimulus such as recent COVID-19 or vaccine. At the end of this survey we aimed to understand better the dynamic of antibodies in KTR.
Re-Initiating Living Donation Kidney Transplantation in Covid-19 Pandemic; Indonesia Experience

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Introduction: Kidney transplantation (KT) is one of many health care procedures impacted by the COVID-19 pandemic and most KT centres decided to withhold their program, especially living kidney transplantation. With 45 years of experience, the KT program in Indonesia’s KT centres in Jakarta was also stopped for a month in April 2020 due to uncertain conditions after the first COVID-19 case was detected in Indonesia in early March 2020 and restarted after adjustments including the COVID-19 prevention protocols were made to adapt to the pandemic era in line with international and national health organizations guideline. The profile, trend, changes for adaptation and safety in regards to preventing COVID-19 infection to the patients of the living donation KT procedures in Indonesia during the pandemic era is not well recorded. Therefore, this study aims to collect and report the data.

Method: In a retrospective cohort study, the detailed report and scheduling of KT procedures from January 2020 to January 2022 in Dr. Cipto Mangunkusumo Hospital and Asri Hospital, Jakarta, Indonesia were collected and assessed to look for the number of performed KT in Indonesia before and during the pandemic era. The data of KT in both hospitals after the program restarted during the pandemic era from May 2020 to January 2022 was the focus of evaluation.

Results: An average of 9.67 KT procedures/month were performed in January-March 2020. No KT procedures were performed in April 2020. 3 KT procedures were done in May 2020 as the KT program was restarted. An average of 8.95 KT procedures/month were performed in May 2020–January 2022. Out of 208 KT schedules from May 2020 to January 2022, 188 KT’s were performed on schedule, 13 were rescheduled or cancelled due to clinical conditions other than COVID-19, while 7 (3.37%) were due to patient’s COVID-19 infection confirmed by PCR during the preoperative hospital stay. 55.32% of donors and 68.09% of recipients were male. Only 5.85% of recipients were paediatrics while the rest were adults. Starting from October 2020, 100% of the laparoscopic approach has been shifted to retroperitoneal from transperitoneal in purpose to minimize the risk of COVID-19 infection from patient to medical staff. Based on the data from Dr. Cipto Mangunkusumo Hospital only, 94% of KT recipients stay uninfected by COVID-19 following their KT procedure until this study is performed, while 6 recipients were infected in which 2 were infected during 14–28 days after the procedure and 4 were infected at more than 14–28 days after.

Conclusion: Indonesia KT centres succeeded to overcome the COVID-19 pandemic situation and is back to safely performing the same normal amount of KT procedures monthly as before the pandemic. The success is the result of some adaptations including COVID-19 screening protocols for the medical staff and patients and a change in the laparoscopic approach.

We would like to thank dr. Irfan Wahyudi as the Head of Department of Urology Dr. Cipto Mangunkusumo Hospital Jakarta, Indonesia for moral and legal aspect support during the data collection and preparation of this abstract. We would like to thank dr. Agustina Suhanura as Director of Asri Hospital Jakarta, Indonesia for legal aspect support during the data collection and preparation of this abstract. We would like to thank dr. Ghifari Nurulhah for his support in collecting the data used in this abstract. We would like to thank dr. Claudio Agustino for his support in collecting the data used in this abstract. We would like to thank dr. Haryo Satrio Muhammad for his support in collecting the data used in this abstract.
Table 1. Screening Timeline for Patients and Operative

<table>
<thead>
<tr>
<th>Day</th>
<th>Activity</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-8</td>
<td>Swab PCR test for the donor and recipient (including 1 guard each)</td>
<td>Outpatient clinic</td>
</tr>
<tr>
<td></td>
<td>Swab PCR test for the perioperative team (intensists, radiologists, psychiatrist, transplant nurses, ICU team, dieticians, porters, cleaning service)</td>
<td></td>
</tr>
<tr>
<td>D-7</td>
<td>Swab results are negative*:</td>
<td>Ward</td>
</tr>
<tr>
<td></td>
<td>- patients check in for hospitalization</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ward team starts preparing the patients</td>
<td></td>
</tr>
<tr>
<td>D-3</td>
<td>Swab PCR test for the surgical team (urologists, anaesthesiologists, OR nurses)</td>
<td>Ward</td>
</tr>
<tr>
<td></td>
<td>Swab PCR test for the donor and recipient</td>
<td></td>
</tr>
</tbody>
</table>

Notes:
*When the result of the PCR SARS-CoV-2 is positive, the transplant process is withdrawn and the protocol for management of positive COVID-19 patients is applied.
**When the result of the PCR SARS-CoV-2 is positive, the protocol for management of positive COVID-19 patients is applied.

A. Number of kidney transplant procedures by Dr. Cipto Mangunkusumo Hospital

B. Demography of total donors of performed KT in both hospitals by gender in Dr. Cipto Mangunkusumo Hospital and Airlangga Hospital, Indonesia, from The Early 2020 to Early 2022

C. Demography of total recipients of performed KT in both hospitals by age in Dr. Cipto Mangunkusumo Hospital and Airlangga Hospital, Indonesia, from The Early 2020 to Early 2022

D. SMR Laparoscopic Approach to Transfused to Retransplanted of performed kidney transplant procedure in Dr. Cipto Mangunkusumo Hospital and Airlangga Hospital Jakarta, Indonesia, from The Early 2020 to Early 2022

E. COVID-19 infection status of KT Recipients following the performed KT procedure in Dr. Cipto Mangunkusumo Hospital, Indonesia, from The Early 2020 to Early 2022

F. Charts showing the distribution of COVID-19 infection status among KT recipients.
SARS-CoV-2 Antibody Response by mRNA Vaccine Platform in Incrementally Immunosuppressed Patients

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Introduction: This study compares SARS-CoV-2 antibody responses between the two-dose mRNA-1273 and BNT162b2 vaccine series across groups of incrementally immunosuppressed patients.

Methods: Semiquantitative testing for antibodies against the receptor binding domain (RBD) of the SARS-CoV-2 spike protein was performed using the Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay (EIA), 15-45 days after the second vaccine dose for SARS-CoV-2 naïve patients with rheumatic and musculoskeletal disease (RMD), and solid organ transplant recipients (SOTRs) from an observational cohort. Anti-RBD titers were divided into categories of ≥50, ≥100 and ≥250 U/mL based on levels associated with plasma neutralizing capacity in COVID-19 convalescent patients. Participants were stratified by increasing intensity of immunosuppression: RMD not on immunosuppression, RMD on immunosuppression, SOTR not on mycophenolate (MMF), and SOTR on MMF. Response rates between mRNA-1273 and BNT162b2 recipients were compared using modified Poisson regression weighted for age, time since vaccination, and number of immunosuppressive medications. This analysis was repeated for several thresholds of positive response: 50, 100, and 250 U/mL.

Results: Of 1868 participants, 55.8% of RMD and 52.7% of SOTRs received BNT162b2; the remainder received mRNA-1273. Demographics, diagnoses, and immunosuppressive regimens were similar across vaccine groups. Among RMD participants not on immunosuppression, the chance of anti-RBD ≥250U/mL was comparable among BNT162b2 and mRNA-1273 recipients (IRR= 0.91 1.03 1.16 p= 0.67). mRNA-1273 recipients had a higher chance than BNT162b2 recipients to achieve anti-RBD ≥250U/mL among RMD participants on immunosuppression (IRR = 1.15 1.24 1.34, p<0.001); SOTRs not on MMF (IRR = 1.24 1.56 1.96, p <0.001); and SOTRs on MMF (IRR= 1.28 2.62 5.37, p= 0.01). Similar trends were observed with titer cutoffs of ≥100 and ≥50 U/mL (Table 1).

Conclusion: The two-dose mRNA-1273 vaccine series was more likely to induce stronger humoral immunogenicity compared to BNT162b2 in immunosuppressed patients; this effect was more pronounced with greater immunosuppression. These findings suggest importance in the choice of mRNA vaccine platform in optimizing immune responses to SARS-CoV-2 vaccination and can help inform vaccination strategies for booster doses in high-risk, immunosuppressed populations.


Table 1. Anti-RBD Response to two-dose mRNA SARS-CoV-2 vaccination stratified by vaccine platform

<table>
<thead>
<tr>
<th>Antibody Titer (U/mL)</th>
<th>% BNT162b2</th>
<th>% mRNA-1273</th>
<th>IRR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMD not on immunosuppression (n=122)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50</td>
<td>98.5</td>
<td>94.4</td>
<td>0.90</td>
<td>0.26</td>
</tr>
<tr>
<td>≥100</td>
<td>94.1</td>
<td>94.4</td>
<td>1.00</td>
<td>0.94</td>
</tr>
<tr>
<td>≥250</td>
<td>88.2</td>
<td>90.7</td>
<td>1.03</td>
<td>0.67</td>
</tr>
<tr>
<td>RMD on immunosuppression (n=1036)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50</td>
<td>77.4</td>
<td>84.5</td>
<td>1.07</td>
<td>0.02</td>
</tr>
<tr>
<td>≥100</td>
<td>74.6</td>
<td>83.8</td>
<td>1.13</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥250</td>
<td>63.6</td>
<td>81.0</td>
<td>1.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SOTR not on MMF (n=260)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50</td>
<td>59.1</td>
<td>78.9</td>
<td>1.38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥100</td>
<td>54.6</td>
<td>77.3</td>
<td>1.47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥250</td>
<td>48.7</td>
<td>66.4</td>
<td>1.56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SOTR on MMF (n=437)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50</td>
<td>12.8</td>
<td>21.8</td>
<td>1.69</td>
<td>0.02</td>
</tr>
<tr>
<td>≥100</td>
<td>7.7</td>
<td>18.8</td>
<td>2.40</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥250</td>
<td>4.3</td>
<td>11.4</td>
<td>2.62</td>
<td>0.01</td>
</tr>
</tbody>
</table>

a. Roche Elecsys anti-RBD po-lg(u) (unit/mL) is considered positive per manufacturer (commercial upper ceiling <250, with later expansion to >2500U/mL).
b. Rheumatic and musculoskeletal diseases include inflammatory arthritis, systemic lupus erythematosus, systemic sclerosis, myositis, Sjogren's syndrome, systemic vasculitis and overlap connective tissue disease as well as chronic non-inflammatory conditions including osteoarthritis, fibromyalgia.
c. Solid Organ Transplant Recipients including liver, kidney, pancreas, lung, heart, intestine and multiple organ transplant.
d. MMF includes mycophenolic acid and mycophenolate mofetil.
Intervention: Patients with kidney failure on dialysis and with kidney transplant are at least five times more likely to die from COVID-19 than patients without kidney disease. Yet, vaccine efficacy in these patients is unclear. Aims: We examined the immunogenicity of BNT162b2 COVID-19 vaccination in Covid-naïve dialysis and transplant recipients using Spike antibody levels.

Methods: Kidney transplant and dialysis patients in a single centre underwent spike antibody testing using the Roche elecsys SARS-CoV-2 Nucleocapsid Total Antibody assay prior to vaccination, at 1 and 3 weeks after the second vaccination dose and at 1 month and 3 months after the third vaccination dose.

Results: 388 patients underwent vaccination, and all had antibody levels tested (162 Kidney Transplant, 226 Dialysis). None had COVID-19 infection prior to vaccination. Mean Covid spike antibody levels were higher in dialysis patients than transplant recipients at week 1 (183.9U/ml versus 39.3U/ml) and week 3 (217.0U/ml versus 55.3U/ml) (p < 0.001 for both comparisons) (Figure 1). Three weeks after vaccination, 32% of transplant recipients had seroconverted compared to 96% of dialysis patients. Transplant recipients were younger than dialysis patients and less co-morbid. There was no association between patient age, sex or time from transplantation with seroconversion in Covid-naïve dialysis and transplant recipients using Spike antibody levels.

Conclusion: Seroconversion rates after 3 doses of the Pfizer SARS-CoV-2 vaccine in Dialysis Patients are lower than in Dialysis Patients. Vaccination prior to transplantation and booster doses in transplant recipients are recommended.

Antibody levels post vaccination

![Antibody levels graph]

249.10 COVID-19 Infection in Liver Transplant Recipients: Results From a Brazilian Multicentric Historical Cohort

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Introduction: Amid the COVID-19 pandemic, the consequences of infection by the SARS-CoV-2 virus in Liver Transplant recipients (LT) patients is of particular concern, notably due to the perceived added risk of these patients related to immunosuppression and comorbidity burden. Current literature on this topic often uses small, non-standardized, and ethnically limited samples. This study describes COVID-19 presentation and complications in a large, multicentric, and ethnically diverse population of LT recipients.

Methods: We designed this study as a multi-centric historical cohort, analyzing patient records submitted by an online questionnaire. The study included LT recipient patients with suspected or confirmed COVID-19 already in follow-up at the study centers. The primary endpoint was COVID-related death. We also collected demographic, clinical, and laboratory data regarding presentation and disease progression.

Results: We included 314 patients from 25 participant centers in Brazil. It is, to our knowledge, the largest current cohort of LT recipients with COVID-19. The median age was 60 years old (IQR: 53-69), and the hospitalization rate was 56%, with an overall mortality rate of 17.9%. Patients were mostly male (66%), white (59%), and overweight, with a median BMI of 27 (IQR 24-33). The median follow-up time was 117 days (IQR 41-291). The two most prevalent comorbidities were hypertension (N= 138 - 44%) and diabetes (N= 129 - 45%). Increased mortality was associated with fewer years from transplantation (p=0.03), increased BMI (p=0.02), the presence of dyspepsia (p<0.001), and lost sense of smell (p=0.01) at presentation, and alterations to immunosuppression after admission (p=0.001). The use of mycophenolate at admission was also associated with increased mortality (p=0.02). Liver function test results were not associated with mortality. Median time from admission to death was 22 days (IQR: 12-35).

Conclusion: This large, multicentric study suggests novel risk factors for mortality not previously reported in other studies - notably the use of Mycophenolate and fewer years from transplantation. As such, the results of this study are paramount to the comprehensive and individualized treatment of this multifaceted patient population and stand as a stepping stone for further understanding of the disease presentation in these patients. Regina G Santos, Laura CM Pinto, Simone R Prata, Letícia Zanaga, Rita CMP Silva, Luiz AC Dalbuquerque, Renata Ferreira Bezerra, Marcelo Nogara, Huda M Nourah, Agnaldo S Lima, Ana P Passos, Valéria RC Brasil, Renato Hidalgo, Christian E Garcia, Alyth K Sankaranthanikky, Adriano M Gonzales, Andre I David, Mauricio Barros, Ben-Hur E Ferraz-Neto, Claudiemiro Quireze-Júnior, Eduardo Fonaica.
Survival After COVID-19 in Liver Transplant Recipients According to Disease Waves - Results From a Brazilian Multicentric Study

Elaine C Atadje1, Tercio Gonsinzi2, Regina G Santos2, Lucio FP Moreira3, Laura CM Pinto3, Raquel SB Stucchi1, Eduardo Riccetto1, Renato F Silva4, Rita CMF Silva5, Luciana Haddad2, Luiz AC Dalbuquerque5, Marcio D Almeida5, Andre Watanabe6, Gustavo PS Melo6, Claudio ML Melo6, Renata F Bezerra7, Nertan L Telfi11, Marcia Halpern11, Andre Watanabe7, Gustavo PS Melo8, Claudio ML Melo9, Eduardo Riccetto1, Renato F Silva4, Rita CMF Silva4, and safe criteria.

In relation to COVID-19 after liver transplantation, however, studies such as waves. As already mentioned, there are no reports of cases similar to ours in the world as well as in Brazil between 2020 and 2021. There are no robust studies describing the profile of liver transplant patients who are victims of COVID-19, especially when it comes to comparing this profile against the waves. We carried out a national multicenter study that can cover a significant number of liver transplant patients and verify the prognostic factors of survival of these patients according to the period of illness by COVID-19.

The main objective of this study was to evaluate factors associated with wave survival in COVID-19 disease, in the postoperative period of liver transplantation. This is a cross-sectional, retrospective study, with analysis of data from the medical records of patients with suspicion or positivity for COVID-19 provided by the coordinators of the Liver Transplantation Groups of Brazil (GTxF-COVID-19/Brazil), through a survey applied online.

In this study, 25 centers were evaluated, totaling 311 patients in the postoperative period of liver transplantation, of which 128 (41.1%) were treated at home and 183 (58.9%) were hospitalized. Of the 183 hospitalized, 54 (hospital mortality of 29.5%) died. The need for mechanical ventilation was 65/183 (35.5%). The prevalence in this study was 311/183x45 (1.9% or 1.900) and mortality was about 29.2 per 100,000 inhab. (17.36%). There were no records of deaths at home.

Evaluating the number of cases according to the waves of COVID-19, we observed that in wave 1 there were 131 cases (47.3%) and in wave 2 there were 146 cases (52.7%). In the two waves, the most frequent symptoms (over 10 cases) were: fever, cough, dyspnea, fatigue, coryza, headache, diarrhea, myalgia and dyspnea. The most frequent comorbidities in both waves were diabetes, hypertension, obesity, smoking, kidney disease and heart disease. The length of stay in ICU days was longer in the first wave (5.72 ± 11.79; p=0.04) than in the second wave. There was a greater number of hospital admissions in the first wave, 70.2% against 53.4% in the second wave (p=0.004). There was a greater number of "pre" COVID-19 treatment (use of hydroxychloroquine, chloroquine and azithromycin) in the first wave (65.6%) compared to the second wave (51.9%) and this difference was significant (p=0.03). There were less management, reduction or withdrawal of immunosuppression in these patients in the second wave (p=0.02).

The actuarial survival curve estimated by the Kaplan-Meier method comparing survival from the onset of symptoms to resolution of the patients’ clinical condition did not show a statistically significant difference between the two waves. As already mentioned, there are no reports of cases similar to ours in relation to COVID-19 after liver transplantation, however, studies such as those presented here are imperative in order to create solid foundations for definitions of the management of this population that requires attention and safe criteria.

The Impact of Monoclonal Antibody Against SARS-COV2 And Vaccination on Outcomes in Kidney Transplant Recipients With COVID-19

Nicole Ali1, Vasishta Tatapudi1, Ranjetta Chand1, Kimberly Sureau1, Sapna Mehta1, Robert Montgomery1, 1Transplant Institute, NYU Langone Health, New York, NY, United States; 2CareDx, CareDx, Brisbane, CA, United States.

Purpose: Solid organ transplant recipients are at high risk of morbidity and mortality from coronavirus disease 2019 (COVID-19) with mortality rates as high as 30% reported in the early pandemic period. COVID-19 vaccine efficacy in the immunosuppressed population is lower than the general population. Early studies suggest that monoclonal antibody (MAB) treatment against the SARS-CoV-2 spike protein may decrease hospitalizations and emergency department (ED) visits. Herein, we report our single center experience with use of MAB for COVID-19 treatment in kidney transplant recipients.

Methods: We performed a retrospective chart review of all kidney transplant recipients who developed COVID-19 from March 17, 2020 to January 26, 2022 at our transplant center. Date of diagnosis, vaccine status, MAB treatment, hospitalization and patient outcome was reviewed.

Results: Two hundred ninety-one kidney transplant recipients had positive testing for SARS-CoV-2 in the period reviewed. 120 (41%) patients received MAB treatment. One patient death which was not COVID related was excluded from analysis. Of patients who received MAB treatment, 92.2% survived compared to 82.4% of those who did not (p=0.00). Figure 1. Hospitalization was lower in those who received MAB (18.3% vs 60.8%, p=0.00). Completion of vaccine series, defined as 2 doses of mRNA or 1 dose of Janssen vaccine prior to infection, was also associated with better survival (86.6% vs 80.3%, p=0.00). Figure 1. Hospitalization rate was lower in those who completed vaccination prior to infection with SARS-CoV-2 (27.1% vs 59.2%, p = 0.00). The combination of MAB therapy and completion of vaccination also decreased hospitalization compared to those who received MAB but did not complete vaccine series (14% vs 26.8%, Table 1). Subgroup analysis of 143 patients infected from December 2021 to Jan 26, 2022 which may have reflected the Omicron surge was performed (Table 2). Treatment with MAB was associated with a reduction in hospitalization (11.6%) compared to 44.6% in those who did not receive MAB.

Conclusion: MAB treatment for COVID-19 and prior vaccination were associated with improved survival and decreased risk of hospitalization in kidney transplant recipients.

Table 1 – Summary of patients by MAB treatment and vaccination status

<table>
<thead>
<tr>
<th>Vaccination Status</th>
<th>MAB treatment (n, %)</th>
<th>No MAB treatment (n, %)</th>
<th>Vaccinated (n, %)</th>
<th>Not Vaccinated (n, %)</th>
<th>MAB + Vaccine (n, %)</th>
<th>MAB, no Vaccine (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized</td>
<td>22 (18.3%)</td>
<td>104 (86.8%)</td>
<td>29 (27.1%)</td>
<td>87 (93.9%)</td>
<td>11 (14.4%)</td>
<td>111 (13.6%)</td>
</tr>
<tr>
<td>Not Hospitalized</td>
<td>90 (81.7%)</td>
<td>17 (15.1%)</td>
<td>15 (27.9%)</td>
<td>60 (60.8%)</td>
<td>48 (59.6%)</td>
<td>30 (36.4%)</td>
</tr>
<tr>
<td>Survival</td>
<td>115 (92.9%)</td>
<td>14 (12.5%)</td>
<td>14 (12.5%)</td>
<td>101 (101%)</td>
<td>47 (56.6%)</td>
<td>40 (48.8%)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (0.8%)</td>
<td>0 (17.6%)</td>
<td>2 (14.3%)</td>
<td>0 (17.6%)</td>
<td>0 (0%)</td>
<td>1 (2.4%)</td>
</tr>
</tbody>
</table>

Table 2 – Summary of patients by MAB treatment and vaccination status infected from Dec 2021 to Jan 26, 2022 (Emergence of Omicron variant)

<table>
<thead>
<tr>
<th>Vaccination Status</th>
<th>MAB treatment (n, %)</th>
<th>No MAB treatment (n, %)</th>
<th>Vaccinated (n, %)</th>
<th>Not Vaccinated (n, %)</th>
<th>MAB + Vaccine (n, %)</th>
<th>MAB, no Vaccine (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized</td>
<td>8 (12.5%)</td>
<td>55 (94.4%)</td>
<td>55 (94.4%)</td>
<td>8 (12.5%)</td>
<td>8 (12.5%)</td>
<td>55 (94.4%)</td>
</tr>
<tr>
<td>Not Hospitalized</td>
<td>56 (87.5%)</td>
<td>3 (5.5%)</td>
<td>2 (3.8%)</td>
<td>54 (87.5%)</td>
<td>54 (87.5%)</td>
<td>3 (5.5%)</td>
</tr>
<tr>
<td>Survival</td>
<td>64 (98.6%)</td>
<td>2 (3.5%)</td>
<td>125 (99.1%)</td>
<td>0 (0%)</td>
<td>64 (100%)</td>
<td>125 (99.1%)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (1.4%)</td>
<td>2 (2.3%)</td>
<td>1 (0.8%)</td>
<td>0 (0.8%)</td>
<td>1 (1.4%)</td>
<td>2 (2.3%)</td>
</tr>
</tbody>
</table>

Figure 1 – Survival and hospitalization by those who receive MAB treatment and vaccination status.
Abstracts310.1
Consequences of Breakthrough COVID-19 Infection in Solid Organ Transplant Recipients Relative to Non-immunosuppressed Controls

Amanda Vinson1, Alfred J. Anzalone2, Jing Sun3, Ran Dai4, Gaurav Agarwal5, Stephen B. Lee6, Evan French7, Amy Olex7, Michael G. Ison8, Roslyn B. Mannon9.
1Medicine, Dalhousie University, Halifax, NS, Canada; 2Neurological Sciences, University of Nebraska Medical Center, Omaha, NE, United States; 3Epidemiology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, United States; 4Biostatistics, University of Nebraska Medical Center, Omaha, NE, United States; 5Medicine, University of Alabama at Birmingham, Montgomery, AL, United States; 6Medicine, University of Saskatchewan, Regina, SK, Canada; 7Virginia Commonwealth University, Richmond, VA, United States; 8Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, United States; 9Medicine, University of Nebraska Medical Center, Omaha, NE, United States.

Introduction: The COVID-19 pandemic has had an immense impact on solid organ transplant (SOT) recipients. COVID-19 vaccination is remarkably effective in the general population; however SOT recipients have an impaired immune response and vaccine efficacy in this immunosuppressed population has been questioned. Most studies of vaccination in SOT recipients to date have primarily examined the immune response to vaccination, with less consideration of the clinical outcomes following breakthrough COVID infection.

Methods: In a cohort of adult patients testing positive for COVID-19 prior to the Omicron wave (12/10/2020-12/18/2021), we used data from 37 sites across the United States using the National COVID Cohort Collaborative (N3C) to examine the efficacy of 2 doses of mRNA vaccination or 1 dose of Johnson & Johnson (VAX2) in a non-immunocompromised/immunosuppressed (ISC) population compared to SOT recipients. The cumulative incidence of breakthrough COVID-19 (BTCo) in the 6 months post VAX2 in the non-ISC population and in the SOT cohort by organ type (kidney, liver, lung, or heart) was demonstrated using cumulative incidence curves per 1000 persons. We assessed the risk of complications (major adverse renal or cardiovascular events (MARCE), major adverse cardiac events (MACE), acute kidney injury (AKI), mortality, hospitalization, or a composite of requiring ECMO, ventilation, or dying) in the 90-days post BTCo in VAX2 SOT recipients versus SOT with unconfirmed vaccination status (UVS) using multivariable Cox proportional hazards and logistic regression as required. This analysis was repeated in the non-ISC population for comparison.

Results: Over the study period, following VAX2, BTCo occurred in 818 (11.5%) SOT recipients and 38,401 (5.7%) non-ISC patients. Median time from vaccination to BTCo was 117 days (IQR 68-145) in the SOT cohort and 127 days (IQR 93-154) in the non-ISC cohort. Lung transplant recipients had the highest cumulative incidence of BTCo, and after non-ISC, and liver transplant recipients had the lowest (Figure 1). The greatest relative benefit with vaccination for both non-ISC and SOT cohorts was in BTCo mortality (HR 0.45, 95% CI 0.43-0.48 for non-ISC and HR 0.62, 95% CI 0.47-0.82 for SOT relative to UVS), and in the composite of needing ECMO, ventilation, or dying (OR 0.28, 95% CI 0.25-0.31 for non-ISC and HR 0.69, 95% CI 0.54-0.88 for SOT relative to UVS), Figure 2.

Conclusion: While the relative benefit of vaccine was less in SOT than non-ISC, SOT patients still exhibited significant benefit with vaccination. Although this study demonstrates moderate benefit in reducing major complications after BTCo in SOT recipients, immunosuppressed patients must remain vigilant of their risk and continue to minimize exposure.
310.2

Mortality of the Patients on the Waiting List for Solid Organ Transplantation During the COVID-19 Pandemic in Argentina

Liliana Bisigniano1, Viviana Tagliafichi1, Daniela Hansen Krogh1, Carlos Soratti2, Ariel Antik1.

1Scientific and Technical Direction, INCUCAI, Caba, Argentina; 2Presidence, INCUCAI, Caba, Argentina.

Introduction: Patients on the solid organ transplant waiting list may be at increased risk of severe acute respiratory syndrome and death from COVID-19. Likewise, there is also a risk when transplanting a patient during the pandemic. The balance between the risks of transplanting over the risks of remaining on the waiting list in periods of high viral circulation of COVID-19, as well as the impact of vaccination, has not been studied in our country. The objective of this study was to determine the incidence of COVID-19 infection in patients on the waiting list for solid organs during the pandemic in Argentina, to compare the mortality from COVID-19 in patients on the waiting list vs. transplant patients, and the effect of vaccination on mortality.

Methods: This study was conducted using a national cohort study. The main source was the Argentine Information Management and Registration System (SINTRA). Three time periods were analyzed: 03/31/20-02/28/21, 03/01/21-11/30/21 and 12/01/2-02/28/22. Mortality rate, prognostic factors and evolution were analyzed by multivariate analysis. For the analysis of the impact of vaccination, it was considered vaccinated if the patient received at least 2 doses.

Results: During the 3 periods analyzed, 10,017 recipients on the waiting list for solid organs were confirmed with COVID-19. The mortality rate was 24% (928/3882); 18% (601/3,332) and 3% (78/2,803) for each period, respectively. The mortality rate in transplant patients was: 20% (310/1,549); 20% (384/1,892) and 3% (66/1,883), for the same periods analyzed. Higher mortality is observed in patients on the waiting list at the first peak of the pandemic (p=0.02). The vaccination rate was 57% and 74% in the 2nd and 3rd periods, respectively. Mortality according to the organ waiting list period was: lung (13%-24%-13%), heart (19%-19%-5%), kidney (24%-18%-2%) and liver (24% - 18%-3%), kidney-pancreas (26%-17%-4%). In the multivariate analysis, the probability of death in waiting list patients was associated with age over 56 years (OR 1.6, 95% CI 1.4-1.9), hospitalization (OR 5.7, CI 4.8-6.6), admission to intensive care (OR 2.8 CI 2.1-3.8), and mechanical ventilation requirement (OR 13.7, 95% CI 8.4-22.3). Vaccination was a protective factor against mortality (OR 0.04, 95% CI 0.03-0.05).

Conclusion: In Argentina, in the first period of the pandemic, a worse evolution of COVID-19 was observed in recipients on the waiting list for solid organ transplants compared to transplant patients. Mortality decreased mainly in the third period mainly due to vaccination and the optimization of prevention and treatment measures for COVID-19.

310.3

Posoleucel as Preemptive Therapy for BKV Infection in Kidney Transplant Recipients: Safety, Tolerability and Efficacy in a Phase 2 Trial

Anil K. Chandraker1, Manpreet Singh2, Anil Regmi3, M. Javeed Ansari4, Bonnie Lonze5, Vinay V. Nair6, Akhil Sharma7, Stuart J. Knechtle8, Francesca Cardarelli9, William Marshall8, David Wojciechowski10, Liliana Bisigniano1, Viviana Tagliafichi1, Daniela Hansen Krogh1, Carlos Soratti2, Ariel Antik1.

1Brigham & Women’s Hospital, Boston, MA, United States; 2University of Pittsburgh Medical Center, Harrisburg, PA, United States; 3Inova Transplant Center, Falls Church, VA, United States; 4Northwestern University Feinberg School of Medicine, Chicago, IL, United States; 5NYU Langone Transplant Institute, New York, NY, United States; 6Northwell Health, Manhasset, NY, United States; 7University of Pittsburgh Medical Center, Pittsburgh, PA, United States; 8Duke University School of Medicine, Durham, NC, United States; 9AlloVir, Waltham, MA, United States; 10University of Texas Southwestern Medical Center, Dallas, TX, United States.

Purpose: Kidney transplant (KT) recipients with BK viremia are at risk for BK virus (BKV) nephropathy and graft loss. There are no approved therapies for BKV infection. Posoleucel (PSL) is an off-the-shelf, allogeneic multivirus-specific T cell therapy that targets BKV as well as adenovirus, cytomegalovirus, Epstein-Barr virus, human herpesvirus 6, and JC virus. In a phase 2 trial of PSL in hematopoietic cell transplant recipients, 100% (27/27) of those with BKV disease had a clinical response.

Methods: We are conducting a phase 2 double-blind placebo (PBO)-controlled study of PSL in 60 KT recipients with BK viremia (NCT04605484) in which patients are randomized 1:1:1 to receive PSL (Groups 1 and 2) or placebo for 12 weeks. PSL (4 x 10^7 PSL cells) is infused once a week for 3 weeks, then every 14 days (Group 1) or every 28 days (Group 2). After these 12-week dosing periods, patients are followed for 12 more weeks (observation period). The primary objective is safety and tolerability with a key secondary objective to assess changes in BK viremia.

Results: This interim analysis of the ongoing study includes the first 37 patients enrolled as of 22 Feb 2022; 29 (78%) patients were male and 8 (22%) were female; 20 (54%) Caucasian, 10 (27%) African American, 4 (11%) Asian, and 3 (8%) were other race or not reported; 3 (8%) patients were of Hispanic ethnicity. Patients’ median age was 58.5 years, with a range from 32 to 75 years. Median day of PSL or PBO initiation post KT was 472 days (range 59 to 5158 days). Mean eGFR at start of the dosing period. The primary objective is safety and tolerability with a key secondary objective to assess changes in BK viremia.

Conclusions: In this ongoing trial—the first randomized, double-blind placebo-controlled therapeutic trial of virus-specific T cell therapy in KT recipients with BK viremia—PSL was generally safe and well tolerated, supporting its continued evaluation as a preemptive therapy in KT recipients at risk for BKV nephropathy.

This study was funded by AlloVir.
Abstracts

310.4

Disparities in Low Respiratory Vaccination Among Solid Organ Transplant Recipients

Jamie Felzer1, Lila J. Finney Rutten2, Chung-Il Wi3, Allison M. LeMahieu2, Elena Beam1, Young J. Juhn3, Robert M. Jacobson3, Cassie C. Kennedy1.

1Medicine, Mayo Clinic, Rochester, MN, United States; 2Quantitative Health Sciences, Mayo Clinic, Rochester, MN, United States; 3Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN, United States.

Introduction:
Influenza is the most common vaccine-preventable infection the first 5 years post-transplant. Despite the availability of safe and effective vaccines, vaccine uptake is low among high-risk transplant patients who are recommended to receive pneumococcal and annual influenza vaccines. While disparities in vaccination have been observed by race, with lower uptake among Blacks and Hispanics, little is known about the role of sociodemographic characteristics including an individual-level housing-based HOUSES index, education, marital status and geographic location (rural/urban classification) play in vaccine uptake. To improve health outcomes and vaccine coverage, we must identify and target populations with low uptake.

Methods:
We conducted a cross-sectional, population-based study using the Rochester Epidemiology Project (REP), a medical records linkage system, to assess sociodemographic factors associated with influenza and pneumococcal vaccination rates among adults aged 19-64 years old with solid organ transplants, living in four counties in southeastern Minnesota. Socioeconomic status (SES) was assessed via HOUSES, measure of SES. Vaccination data was obtained from the Minnesota Immunization Information Connection (MIC) from June 1, 2010-June 30, 2020. Influenza vaccination rate was assessed with Poisson regression models, offset by number of vaccines eligible for; pneumococcal status was assessed with logistic regression models.

Results:
468 solid organ transplant patients were identified (Table 1). Liver and lung transplant patients were least vaccinated for influenza. Influenza vaccination ranged from 52-58% over the past 10 years which was slightly higher than national averages and adults in our area who were recommended to receive pneumococcal vaccines (35-43%). Race was not significantly associated with influenza vaccine uptake when adjusted for geographic region or SES as assessed by HOUSES. If patients were up-to-date on pneumococcal vaccine they had a 26% higher influenza vaccination rate. Heart transplants recipients were least up-to-date on pneumococcal vaccines. 56% of patients were compliant with pneumococcal vaccines, with a median of 18 months under vaccinated. Those living in urban settings were significantly better vaccinated for both influenza and pneumococcus even when adjusted for all other variables (Table 2).

Conclusions:
Rates of vaccination were well below national goals, even though transplant recipients did better than other national estimates of this high-risk group. The transplant process includes rigorous review of vaccinations with close follow-up, and despite this many patients remained under vaccinated. Further investigation is needed to understand and address barriers to vaccination among transplant recipients. This is especially important among subgroups with particularly low rates of adoption, seen particularly in those outside urban areas.

Table 1. Patient demographics (N=468)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at index, median (IQR)</td>
<td>50.2 (39.6, 57.2)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>203 (43.4%)</td>
</tr>
<tr>
<td>Male</td>
<td>265 (56.6%)</td>
</tr>
<tr>
<td>Transplant type, n (%)</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>67 (14.3%)</td>
</tr>
<tr>
<td>Kidney</td>
<td>326 (69.7%)</td>
</tr>
<tr>
<td>Liver</td>
<td>136 (29.1%)</td>
</tr>
<tr>
<td>Lung</td>
<td>33 (7.1%)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>21 (4.5%)</td>
</tr>
<tr>
<td>Black</td>
<td>22 (4.7%)</td>
</tr>
<tr>
<td>Hawaiian/Islander</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Native American</td>
<td>3 (0.6%)</td>
</tr>
<tr>
<td>Other/Mixed</td>
<td>35 (7.5%)</td>
</tr>
<tr>
<td>Refused/Unknown</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>White</td>
<td>387 (82.7%)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>32 (6.8%)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>436 (93.2%)</td>
</tr>
<tr>
<td>Geographic region, n (%), N=432</td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>350 (81.0%)</td>
</tr>
<tr>
<td>Suburban</td>
<td>51 (11.8%)</td>
</tr>
<tr>
<td>Rural</td>
<td>31 (7.2%)</td>
</tr>
<tr>
<td>HOUSES index, n (%), N=429</td>
<td></td>
</tr>
<tr>
<td>Lowest SES (Q1)</td>
<td>121 (28.2%)</td>
</tr>
<tr>
<td>Second Lowest (Q2)</td>
<td>115 (26.8%)</td>
</tr>
<tr>
<td>Second Highest (Q3)</td>
<td>111 (25.9%)</td>
</tr>
<tr>
<td>Highest SES (Q4)</td>
<td>82 (19.1%)</td>
</tr>
<tr>
<td>Marital status, n (%), N=412</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>111 (26.9%)</td>
</tr>
<tr>
<td>Married</td>
<td>240 (58.3%)</td>
</tr>
<tr>
<td>Divorced</td>
<td>53 (12.9%)</td>
</tr>
<tr>
<td>Widowed</td>
<td>6 (1.5%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Education level, n (%), N=449</td>
<td></td>
</tr>
<tr>
<td>8th grade or less</td>
<td>6 (1.3%)</td>
</tr>
<tr>
<td>Some high school</td>
<td>12 (2.7%)</td>
</tr>
<tr>
<td>High school/GED</td>
<td>83 (18.5%)</td>
</tr>
<tr>
<td>Some college or 2-year degree</td>
<td>172 (38.3%)</td>
</tr>
<tr>
<td>4-year college degree</td>
<td>70 (15.6%)</td>
</tr>
<tr>
<td>Post graduate studies</td>
<td>106 (23.6%)</td>
</tr>
<tr>
<td>Smoker, n (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>179 (38.2%)</td>
</tr>
<tr>
<td>No</td>
<td>289 (61.8%)</td>
</tr>
</tbody>
</table>

*133 patients are in multiple transplant groups
Torque teno virus Titre Changes Under Immunosuppression Reduction Protocol for BK Virus-Associated Nephropathy: A Single Centre Pilot Study

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Introduction: In BK virus-associated nephropathy (BKVaN), balancing the risk of immunosuppression (IS) reduction with the potential benefits can be challenging. A common approach is to empirically stop antiproliferative agents in the first instance and reduce the dose of calcineurin inhibitors (CNIs) later. Torque Teno virus (TTV), a novel ubiquitous DNA virus, has emerged as a better predictor of IS burden in some studies. We examined the changes in BKV and TTV titres in response to IS reduction as part of BKVaN treatment.

Method: 20 renal transplant patients with stored blood samples were included in the study cohort from a population transplanted between 2017-19, in remission from an episode of clinically significant BK viraemia. They received standard IS; tacrolimus, antiproliferative (mycophenolate mofetil/azathioprine) and weaning dose prednisolone. BKV and TTV titres, 30-day average tacrolimus concentration, the dose of antiproliferative and prednisolone were collected at 4-time points. These included the last negative BK PCR; the onset of viraemia; the peak BK titre and BK titre <500 copies/ml. TTV DNA was extracted from stored frozen plasma and PCR was performed with Thermofisher 7500 Fast platform and TTV R-GENE® kit. The relationships between the variables were assessed using a multivariable linear regression model. Data were collected from electronic patient records and analysed with R 4.0.3.

Result: The log-transformed mean TTV titre at the 4 time points were 5.02 (2.07), 5.52 (1.74), 6.23 (2.14) and 4.56 (1.27) respectively. In the multivariable model, log-transformed BK virus titre increased by 0.25 for every 1 ng/mL increase in tacrolimus concentration (p 0.0008). However, every 1 log rise in TTV titre led to 0.57 (0.17) log copies increase in BKV titre (p 0.0009), once adjusted for tacrolimus concentration. The relationship between tacrolimus and BKV became statistically insignificant when TTV titre was added as a predictor variable. This implies that TTV titre is a more sensitive predictor of BK viral load than tacrolimus concentration. Although statistically significant, all changes in antiproliferative or prednisolone dose were unable to predict linear changes in BKV titres. 5 patients who lost their graft in the mean follow up of 2.8 years had significantly low TTV titres (p< 0.05) at baseline, indicating suboptimum IS burden. In this small cohort, there was no relationship between TTV titres and rejections (n=5) or de novo DSA (n=3). An ongoing adequately powered prospective study will address these questions more decisively.

Conclusion: Our study demonstrates that TTV titres more accurately indicate the effect of IS/CNI changes on BK titre and demonstrates its potential as a sensitive assay to objectively guide IS modification compared to current empirical practice in the management of BKVaN. A randomised control trial is warranted comparing empirical practices to TTV titre guided adjustment of immunosuppressive medications.
Association of Human Leukocyte Antigen With Anti-sARS-cov-2 Spike Protein Humoral Response

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Introduction: Cellular and humoral response are required for the SARS-CoV-2 eradication. Antigen presenting cells load SARS-CoV-2 peptides on human leukocyte antigen with different avidity and present to T and B cells for the differential humoral and cellular response. Due to immunosuppression, renal transplant recipient patients are speculated to poorly form the antibody against SARS-CoV-2 virus. Therefore, determining the association of specific HLA alleles with anti-SARS-CoV-2 spike protein antibody formation will be helpful in managing the renal transplant recipient patients having specific HLA alleles from SARS-CoV-2 infection and vaccination.

Material and Methods: In this study anti-SARS-CoV-2 spike protein antibody in 161 renal allograft recipient patients were determined by the chemiluminescent microparticle immunoassay methods and human leukocyte antigen alleles were determined by the polymerase chain reaction-single strand oligonucleotide methods and analyzed to study, the HLA alleles association with anti-SARS-CoV-2 spike protein humoral response and severity of COVID-19 symptoms in recently SARS-CoV-2 infected patients. Seroconversion was defined if anti-SARS-CoV-2 spike protein antibody titer was >50AU/ml.

Results: The anti-SARS-CoV-2 spike protein antibody seroconversion rate in renal allograft recipients was 90.06% with median titer 751.80 AU/ml. The frequency of HLA class I alleles A*11 was in 22.1%, A*24 in 21.37%, A*33 in 20.68%, HLA B*15 in 11%, B*07 in 8.27%, HLA-C*30 in 20.93% and C*70 in 23.25% and Class II HLA alleles -DRB1*07 was in 18.62%, DRB1*04 in 13.8%, HLA-DRB1*10 in 14.48% and HLA-DQA1*50 in 32.55% of patient and were associated with the seroconversion.

HLA-B*04, B*52, and B*55 were associated with non-seroconversion in 18.75%, 12.5 and 6.25% of patients respectively, HLA- C*07, C*12, C*30 in 16.6% of patients and C*60 in 33.3% of patients were associated with non-seroconversion. HLA-DRB1*01, HLA-DRB1*03 in 12.5% and DRB1*70 in 6.25% of patients were associated with non-seroconversion. The mean post-infection time of patients recovery from COVID19 symptoms was 18.25±8.14 days.

Conclusion: Renal transplant recipients with SARS-CoV-2 infection developed a robust seroconversion rate of 90.0% and different alleles of HLA-B, DRB1 and DQA1 were significantly associated with the seroconversion.
Disease Classification Risk Through Machine Learning Algorithms – Lessons Learned From COVID-19

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Introduction: SARS-CoV2 virus disease registered more than 460,000,000 confirmed cases worldwide. Mortality due to SARS-CoV2 infection was higher in solid organ transplant recipients (SOT; 10-35% vs 5-7% in general population). We evaluated the utility of applying machine learning (ML) algorithms to a broad database (IDOTCOVID) aiming at developing tools which may be applied to other evolving clinical settings in the SOT field.

Method: We developed and compared 9 different ML models to predict the survival of SOT recipients infected with coronavirus. Models were run on IDOTCOVID, a worldwide database including 1400 patients from 78 transplant centers in 11 different countries between March 2020 and March 2021. Variables included both demographic and transplant related, as well as epidemiological, clinical manifestations, and treatment management of SOT’s with COVID-19. These prediction models include k-nearest neighbors (K-NN), linear regression, SVM with linear kernel, SVM with RBF kernel, two tree-based methods (decision tree, random forests), and three boosting methods (LogitBoost, AdaBoost, XGBoost). After a thorough evaluation, the best predictive machine learning model was used to predict patient survival status. A combined framework of machine learning algorithm and SHAP (SHapley Additive exPlanations) approach was built to provide the comprehensive interpretability of the model, including the discovery of important factors and an analysis of how individual important factors affect prediction outcomes and identification of the corresponding thresholds.

Result: Overall XGBoost achieved the best prediction performance for patient survival among all the algorithms, achieving an AUC of 0.842 (The Area Under the Curve). In the analysis of SHAP values for individual significant factors, three major categories emerged as significant for patient survival – infection period, recipient age, and transplant vintage. In comparing the survival of different patient subgroups, XGBoost performance was better for infections occurring during the first wave (until June 2020; AUC 0.842) than in subsequent waves (AUC 0.755). Conversely, XGBoost performance was better for younger patients (<60 years old; AUC 0.869) than for older patients (AUC 0.773) (Figure 1). Finally, the SHAP analysis identified a U shape curve for patient survival according to time from transplantation, with recipients with an interval of less than 220 days or more than 5.2 years presenting an increased risk of death from COVID-19 disease (Figure 2).

Conclusion: The use of ML was able to accurately assess and predict the survival of recipients following SARS-CoV2 infection. XGBoost provided the best prediction results and may be regarded as an appropriate method for this task. The combination of prediction models and SHAP in broad up-to-date databases may help healthcare professionals identify and modulate important risk factors in evolving diseases.
OVID-Related Neonatal Cholestasis? Liver Transplantation in Three Infants With Perinatal COVID Exposure

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Introduction: The COVID pandemic presents a unique set of challenges during pregnancy including thromboembolic complications, direct placental infection, transplacental transmission, and systemic hyperinflammatory state. Post-COVID cholangiopathy leads to marked cholestasis with ongoing jaundice that persists long after other organs have recovered from infection. We identified a cohort of infant patients who had perinatal exposure to SARS-CoV-2 and then were found to have significant neonatal cholestasis of undetermined cause. These patients underwent orthotopic liver transplant and we present here a potentially new cause of neonatal cholestasis related to SARS-CoV-2.

Methods: Retrospective case review of three infants with perinatal SARS-CoV-2 exposure in 2020 who had persistent cholestasis and extrahepatic biliary obstruction (mimicking biliary atresia), suggesting cholangiopathy, and histologic review of explant liver pathology.

Results: All three patients described in this case series had perinatal exposure to SARS-CoV-2 in 2020 and developed liver failure shortly after birth in the setting of low GGT cholestasis with histologic evidence of extrahepatic biliary obstruction. All three required liver transplantation within the first year of life during 2021.

Conclusion: Though post-COVID cholangiopathy is described in adults in the literature, our series is unique in that it is the first to describe this phenomenon in infancy, with two insults presumably occurring in utero. Additionally, none of our infants had moderate or severe COVID infection but still progressed to advanced liver disease requiring liver transplant. Though further studies are needed to prove causality, our case series certainly raises the question that SARS-CoV-2 may cause in utero or early life insults to the developing liver that may lead to cholangiopathy and end stage liver disease.

<table>
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<th>Table 1. Comparative explant pathology</th>
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<td>Extravascular</td>
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<td>Portal vein</td>
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Intrahepatic Pathology

| Portal fibrosis | Stage 4 | Stage 4 | Stage 4 | Tafreshi, Roth |
| Ductular reaction | Marked | Marked | Marked | Tafreshi, Roth, Lagana |
| Duct loss | Yes | Yes | Yes | Roth |
| Cholangiocytic injury | No | Yes | No | Roth |
| Bile duct plug | Yes, diffuse | Yes, few | Yes, diffuse | - |
| Bile lakes | Yes | No | Yes | Durazo, Tafreshi |
| Microabscesses | No | No | No | Durazo |
| SC-like lesions | No | Yes | No | Durazo |
| Cholestasis | Marked | Marked | Marked | Tafreshi, Lagana |
| Steatosis | No | No | No | Lagana |
| Acute liver injury | No | No | No | Lagana |
| Reg nodules | Yes | Yes | Yes | - |
| Giant cell change | Focal, minimal | Diffuse | Diffuse | - |
| Sinusoidal thrombi | No | No | No | Lagana |
| OPV | Yes | No | Yes | Durazo, Roth, Lagana |
| Microcystic change | No | No | No | Durazo, Roth, Lagana |
| CV thrombi | No | No | No | Roth, Lagana |
310.9

Ultra-Short Duration Pangenotypic Direct Acting Anti-viral Prophylaxis to Prevent Virus Transmission From Hepatitis C Viremic (HCV) Donors to Hepatitis C Negative Kidney Transplant Recipients

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Division of Nephrology and Hume-Lee Transplant Center, Virginia Commonwealth University, Richmond, VA, United States.

Purpose: Previous studies have shown that HCV D+/R- kidney transplantation is feasible using 8-12 weeks of DAAAs. Utilization of abbreviated regimens may obviate the need for insurance approval and delay in therapy. We have previously shown very low transmission rates with a prophylactic peri-operative 7-day DAA (Sofosbuvir/Velpatasvir; SOF/VEL) regimen for ‘kidney-only’ transplants. Ezetimibe, a cholesterol lowering drug, has been shown to restrict HCV entry in hepatocytes in a humanized mouse model. Two published studies suggest that ezetimibe may be synergistic in reduction of HCV transmission from donors to recipients. Here we report our extended experience on 115 D+/R- kidney transplants with or without the addition of ezetimibe to the prophylactic regimen to investigate this effect.

Methods: Data were collected via an Ethics Board approved prospective registry (REFORM/HEPC). Inclusion criteria included: a) De-novo transplant; b) cPRA ≤50%; c) absence of synthetic liver dysfunction; and c) absence of active viral hepatitis. The primary outcome was donor HCV transmission at 90 days post-transplant. Patients were screened with HCV NAT at Day 7, 14, 28 and 90 post-transplant. All subjects received an initial dose of sofosbuvir/velpatasvir (SOF/VEL) +/- ezetimibe on day 0 ≤6 hours prior to transplant and then daily for a total of 7 days. Immunosuppression included induction with rabbit anti-thymocyte globulin followed by maintenance tacrolimus, mycophenolate and steroids. The protocol mandated initiation of full-course DAA therapy in case of 2 consecutive positive NAT tests.

Results: A total of 115 D+/R- transplants (mean age=56 yrs) were included from May 2019-August 2021. The distribution of patients across the two groups was Group 1 (7 days prophylaxis with SOF/VEL alone; N=32) and Group 2 (7d prophylaxis with SOF/VEL plus ezetimibe; N=83). Patients enrolled in the two groups were demographically similar. Five patients (5/115; 4.3%; 95%CI:2%-10%) developed HCV viremia [1/32 (3%) in group 1, and 4/83 (4.8%) in group 2]. The donor genotypes (GT) are as follows: 3/5 (60%) GT3; 1/5 (20%) GT1b; 1/5 (20%) GT2b. All 5 patients with HCV transmission showed stronger association with BPAR as compared to C0 when using correlation plots (not shown). In KTRs with low IPV lower levels of tac were better tolerated with regards to BPAR as compared to high IPV.

Conclusion: BPAR beyond first year is uncommon in KTRs. KTRs were grouped in low and high intra-patient variability (IPV) by protocol and on indication between 6-18 months) were available from 475 KTRs. KTRs were grouped in low and high intra-patient variability (IPV) by the median. Primary outcome was BPAR between year 1-3 posttransplant. Hazard ratios (HR) and confidence intervals (CI) of tac and mpa exposure were adjusted for human leukocyte antigen (HLA)-mismatch and other transplant characteristics.

Results: A total of 16 out of 475 (3.4%) KTRs experienced BPAR between year 1-3 post-transplant. Incidence of BPAR in KTRs with high and low IPV was 5.0% vs 1.3% (p=0.01). Tac was significantly associated with BPAR within year 1-3 post-transplant with an unadjusted HR (uHR) of 0.61 (95%CI: 0.49-0.76; p<0.001) and adjusted HR (aHR) of 0.54 (95%CI: 0.40-0.70; p<0.001) for every 20 µg/L increase in C0, and an uHR of 0.55 (95% CI: 0.42-0.73; p<0.001) and aHR of 0.44 (95% CI: 0.30-0.66; p<0.001) for every 20 µg*h/L increase in AUC0-12h. AUC0-12h-mpa was not associated with BPAR. Probability of BPAR increased exponentially when C0 or AUC of tac was below respectively 5 µg/L or 75 µg*h/L (Figure 1). Escalation of Tac levels above 7 µg/L did not lead to meaningful further reduction in BPAR. AUC showed stronger association with BPAR as compared to C0 when using correlation plots (not shown). In KTRs with low IPV lower levels of tac were better tolerated with regards to BPAR as compared to high IPV.

Conclusion: BPAR beyond year 1 posttransplant is uncommon in KTRs on triple therapy with tac, mpa, and prednisolone after year 1 posttransplant. Trough levels (C0) and area-under-the-curve (AUC0-12h) measurements for tac and mpa (performed per protocol and on indication between 6-18 months) were available from 475 KTRs. KTRs were grouped in low and high intra-patient variability (IPV) by the median. Primary outcome was BPAR between year 1-3 posttransplant. Hazard ratios (HR) and confidence intervals (CI) of tac and mpa exposure were adjusted for human leukocyte antigen (HLA)-mismatch and other transplant characteristics.

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To our knowledge, this is the first study that investigated the impact of tac and mpa exposure beyond the first year posttransplant, which may contribute to better define the therapeutic target window.
Optimizing tacrolimus (TAC) exposure and/or using angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARB) may modulate inflammation (i) as well as interstitial fibrosis and tubular atrophy (IFTA) after kidney transplant (KTx). Two-year data from a study in KTx patients receiving prolonged-release TAC coupled with either ACEi/ARB or other antihypertensives (OAHT) showed that low-dose TAC coupled with ACEi/ARB was associated with less IFTA severity and progression, less IFTA plus i, and delayed onset of clinical rejection compared with low-dose TAC without ACEi/ARB (Cockfield et al. Am J Transplant 2019;19:1730–44). We now report 5-year results from this study.

Methods: This was a Canadian multicenter, prospective, open-label, controlled study in adult de novo KTx recipients randomized in a 2x2 design to standard dose (0.15–0.20 mg/kg) or low dose (LOW; 0.05–0.15 mg/kg) prolonged-release TAC combined with either ACEi/ARB or OAHT. All patients received basiliximab induction, mycophenolate mofetil and prednisone.

Results: Overall, 281 patients were randomized. Between 3 and 5 years, mean TAC trough levels were ~6 ng/mL. Patient survival at 5 years was 94.3% (89.7% in the LOW+OAHT group vs 94.4–95.7% and comparable between groups (94.2–97.2% across groups). Graft function, blood pressure, and proteinuria were similar in all groups. At 5 years, class II dnDSA incidence was 13.2% in the LOW+OAHT group vs 5.6–7.2% in other groups. There were no unexpected safety findings observed at 5 years.

Conclusion: KTx patients receiving low-dose prolonged-release TAC combined with ACEi/ARB have comparable outcomes to those receiving standard doses of prolonged-release TAC with or without ACEi/ARB, while treatment with low-dose prolonged release TAC without ACEi/ARB may be associated with worse outcomes.

This study was sponsored by Astellas Pharma Inc. Editorial support was provided by Cello Health MedErgy, funded by Astellas Pharma Inc.
Every 2-Month Belatacept Maintenance Therapy in Kidney Transplant Recipients: 3-Year Follow-up of a Randomized, Non-inferiority Trial

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1Emory Transplant Center, Emory University, Atlanta, GA, United States; 2Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, GA, United States.

Introduction: Maintenance immunosuppression with belatacept following kidney transplantation results in improved long-term graft function as compared to calcineurin inhibitors. However, broad application of belatacept has been limited, in part related to logistical barriers surrounding a monthly (q1m) IV infusion requirement. Our center conducted a randomized, non-inferiority trial comparing every 2-month (q2m) dosing to standard q1m maintenance. At twelve month follow up, q2m dosing was noninferior to standard q1m dosing as determined by renal function (eGFR). Two-month dosing was safe and well tolerated without a significant incidence of immunologic events in subjects adherent to the study protocol, but longer term follow-up is of interest to better elucidate patient and graft outcomes. Here, we present the 3-year outcomes from this study.

Methods: Low immunologic risk, stable renal transplant recipients a minimum of 1 year post-transplant were randomized to q1m or q2m belatacept maintenance therapy. 36-month follow-up was conducted as intention-to-treat on the population that initiated the study protocol. An autoregressive model using baseline-adjusted means with a random effect for subject was used to compare renal function between groups. Kaplan Meier survival analysis was performed for analysis of adverse and immunologic events.

Results: 163 patients initiated the study protocol and received treatment in the q1m control group (n=82) or q2m study group (n=81). Renal allograft function as measured by baseline adjusted eGFR was not significantly different between groups at 36 months (mean [95% CI], q1m: 73.43[70.37, 76.49] vs. q2m: 72.46[69.08, 75.84].

There were no statistically significant differences in time to death or graft loss (cumulative survival at 36 months, q1m: 92.6%, q2m: 95.0%, p=0.49; freedom from rejection (q1m: 98.7%, q2m: 92.4%, p=0.06), or freedom from DSA (q1m: 98.7%, q2m: 92.4%, p=0.06). During the extended 12-36 month follow-up period, 3 deaths, 1 graft loss occurred in the q1m group, compared to 2 deaths, 2 graft losses in the q2m group. In the q1m group, one patient developed DSA and acute rejection. In the q2m group, 3 patients developed DSA, 2 associated with acute rejection. All acute rejections in both groups were associated with documented medication nonadherence.

Conclusions: Based on similar renal function and adverse event rates at 36 months compared to q1m, q2m belatacept is a viable and safe maintenance immunosuppressive strategy in low immunologic risk kidney transplant recipients with potential to facilitate increased clinical utilization of costimulation blockade-based immunosuppression. (ClinicalTrials.gov NCT02560558)

Modelling of Kidney Allograft Function Depending on Fast Tacrolimus Metabolizer Status at Different Times Post-transplantation

Christophe Masset1,2, Florent Leborgne3, Magali Giral1,2, Claire Garandeau1, Clarisse Kerleau1, Aurélie Houzet1, Diego Cantarovich1, Gilles Blanco1,2, Jacques Dantal1,2, 1Service de Néphrologie et Immunologie Clinique, Institut de Transplantation Urologie Néphrologie, Nantes, France; 2Center for Research in Transplantation and Translational Immunology, UMR 1064, Université de Nantes, Nantes, France; 3INSERM UMR 1246 - SPHERE, Research in Transplantation and Translational Immunology, UMR 1064, Université de Nantes, Nantes, France.; DIVAT Nantes Consortium.

Background: Fast Tacrolimus Metabolizers (FTM+) kidney transplant recipients (KTR) had a lower allograft function due to an important Tacrolimus toxicity. Characterization of FTM+ patients (i.e. C0 Tacrolimus/Dosage of Tacrolimus < 1.05) can be difficult to assess in real life setting due to important dosages modifications in the first months post-transplantation. We investigated the average estimated Glomerular Filtration Rate (eGFR) and its evolution depending on FTM+ status according to the time post-transplantation.

Methods: eGFR up to 5-years post transplantation was analyzed using a linear mixed effect model with random KTR-specific intercepts and slopes in all KTR with a functional allograft at 1-month post-transplantation and undergoing Tacrolimus. The main analysis was performed at T*=1-month; we also studied sub-cohorts at T*=2 to 6-months.

Results: 2025 patients were analyzed at T*=1-month, 45.6% were FTM+. The confounder-adjusted mean eGFR was lower for FTM+ (<4.06 ml/min, 95%CI from -5.57 to -2.55) and the increasing in eGFR level during the first six months was reduced for FTM+; meaning that being FTM+ at T*=1-month lead to a 45% reduction of allograft function improvement between one- and 6-months post-transplantation added to the baseline difference. Using later definition of the FTM+ status (T*>1-month) resulted in comparable results except that the long-term decrease of eGFR was significatively affected when defined from the fifth month post-transplantation.

Conclusion: FTM+ status’ deleterious effect on eGFR occurs since the first month with an eGFR impairment increasing in time. Physicians may consider an immunosuppression adaptation in the very early post-transplantation period to improve allograft function of FTM+ patients.

The Effect of Tacrolimus and Mycophenolic Acid on TTV Loads in Kidney Transplant Recipients

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Background: Measuring immune function in kidney transplant recipients (KTRs) remains challenging given the precarious balance between over- and underimmunosuppression. This is primarily due to high inter- and intrapatient variability in pharmacokinetics and -dynamics of both tacrolimus (TAC) and mycophenolic acid (MPA) and their narrow therapeutic window. Torque teno virus (TTV), a non-pathogenic commensal virus, has been proposed as a marker of immune function: high loads may correspond to over-immunosuppression, and low loads to under-immunosuppression. An inverse relation between TTV load and acute rejection has already been shown. This study aimed to investigate the effect of TAC and MPA exposure on TTV loads in KTRs.

Methods: A cross-sectional cohort study was designed using a unique database of drug exposure data. KTRs transplanted between 2005-2012 and started on TAC/MPA/prednisolone were included. Patients without exposure data, without available samples for TTV load measurement or switches in therapy were excluded, leaving 170 KTR for analysis on Month 3 and 159 on Month 6. Linear regression was used to study the association between TTV loads and TAC through (C0) levels, and TAC and MPA area-under-the-curve (AUC) data, measured on the day of, and 2 weeks before TTV load measurement. Analyses were adjusted for donor and recipient age and gender, number of human leukocyte antigen (HLA) mismatch, days on dialysis, and induction therapy.

Results: Linear regression showed an increase in predicted TTV load at month 3 with TAC C0 and AUC increase in the univariate analysis (C0: β=0.20 per 1 μg/L, p=0.01, R2=0.04); AUC: β=0.18 per 20 mg*h/L, p=0.05, R2=0.04), but not in the analysis adjusted for confounders (C0: β=0.16 per 1 μg/L, p=0.15, R2=0.08); AUC: β=0.01 per 20 mg*h/L, p=0.17, R2=0.08) for exposure samples taken on the same day as the TTV sample. Similar results were found when using samples taken 2 weeks before. For MPA no association was found. Analyses on month 6 showed similar results.

Conclusions: An association between tacrolimus and mycophenolic acid levels and TTV levels was not found in the present study. The low R² values and absence of an association in the adjusted analyses indicate that the high variation in TTV loads is not explained in a linear relationship with drug exposure levels, nor the known covariates. Future study will investigate different timeframes, non-linear relationships and drug exposure and TTV trajectories over time.
Outcomes of Preemptive Second Kidney Transplant by Induction Type in the United States

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Background: The role of induction in preemptive second kidney recipients is unclear. We examined the association between induction therapy and the long-term graft and recipient survival in the settings of tacrolimus and mycophenolate maintenance.

Methods: We identified all preemptive second kidney transplant recipients between 2000 and 2020 in the Scientific Registry of Transplant Recipients. We excluded those with missing or mixed induction regimens and positive crossmatch. We grouped recipients by induction type into three groups: Anti-thymocyte globulin (n=1442), Alemtuzumab (n=362), IL-2 Receptor Antagonist (n=481). We generated Kaplan-Meier curves of the recipient and death-censored graft survival (DCGS) with follow-up censored at ten years. We used multivariable Cox Proportional Hazards models to examine the association between induction and the above outcomes. We adjusted the models for recipient and donor variables.

Results: Rates of delayed graft function (DGF), rejection, hospitalization, and post-transplant lymphoproliferative disorder (PTLD) at one year were not statistically different. Recipient survival did not vary by induction type in the Kaplan-Meier analysis (log-rank P=0.189) or in the multivariable model. However, DCGS was the lowest in the Alemtuzumab group (log-rank P=0.01). In the multivariable models, alemtuzumab was associated with a 57% increased risk of graft loss [1.57, 95% C.I. (1.08, 2.30), P=0.019] compared to anti-thymocyte. Live-donor kidneys were associated with significantly better recipient survival [aHR 0.67, 95% C.I. (0.51, 0.89), P = 0.005] and DCGS [aHR 0.55, 95% C.I. (0.40, 0.76), P < 0.001].

Conclusion: Compared to anti-thymocyte induction, alemtuzumab, but not IL-2RA, was associated with inferior graft survival in preemptive second transplant recipients discharged on tacrolimus and mycophenolate.

IgG and IGG4 Positive Plasma Cell Profile in Recurrent Antibody-Mediated Rejection (AMR) of Cardiac Transplants

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Introduction & Aim: We were curious about the relationship between recurrent antibody-mediated rejection of cardiac transplants and the proportion of total IgG-positive plasma cells in the inflammatory infiltrate and IgG4 subtype, and we planned a preliminary study.

Patients and Methods: 14 endomyocardial biopsy specimens from 12 patients whose clinical course with recurrent suspected or overt AMR and/or acute cellular rejection (ACR) attacks, performed at Baskent University were examined. Some biopsies from these patients, histopathologically diagnosed with acute rejection were selected, and immunoglobulin-G (IgG) and IgG4 stained immunohistochemical. And the frequency, ratio, and profile of plasma cells were evaluated in 1 high magnification area where the most concentrated inflammation area. PRA screening and DSA detection was performed by LUMINEX method (One lambda. Inc., Canoga Park, CA, USA) and MFI 1.000 ≥ was considered positive.

Results: The proportion of IgG positive plasma cells exceeded 10% of the inflammatory infiltrate, for all cases. Although all biopsy sites were screened, no positive plasma cells were detected in the controlled IgG4 immunostaining. We noticed that there was an interesting positive correlation between IgG positive plasma cell count/HPF and anti HLA antibodies mean fluorescence intensity (MFI) values (Table 1).

Discussion: These findings brought to mind the newly defined ‘plasma cell-rich acute rejection (PCRAR),’ which has been associated with poor allograft prognosis in renal transplants. Plasma cell ratios in allograft hearts may be associated with a chronic insidious clinical course. For this reason, it may be possible to determine a meaningful threshold value for plasma cell count with controlled studies in larger case series.
Nurse-Involved Intervention Strategies for Medication Compliance in Kidney Transplant Recipients: A Systematic Review

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Objective: To evaluate the intervention strategies for medication compliance of kidney transplantation recipients with nurses’ participation systematically, and to provide evidence-based evidence for nursing staff to formulate intervention strategies.

Methods: BMJ Best Practice, UpToDate, Joanna Briggs Institute, The Cochrane Library, Guidelines International Network, Registered Nurses’ Association of Ontario, Scottish Intercollegiate Guidelines Network, National Guideline Clearinghouse, PubMed, EmBase, Web of Science, CNKI, WangFang Data. Sinomed were searched to collect evidence of nurse-involved intervention strategies for medication compliance in kidney transplant recipients. The time limit for the retrieval is from the inception of databases until August 7, 2021. 2 researchers screened studied, extracted the data and evaluated the quality of included studies independently.

Results: A total of 22 randomized controlled trials were included in this study. At present, the intervention strategies for medication compliance of kidney transplant recipients with nurses’ participation involving clinical pharmacological care, behavioral intervention, education, electronic monitoring and reminder, telemedically supported case management, cognitive behavioral therapy, mobile drug manager application, etc.

Conclusion: Nursing staff should pay attention to the poor medication compliance of kidney transplant recipients with nurses’ participation systematically, and use existing evidence-based evidence to help kidney transplant recipients improve medication compliance. Caregivers could consider cognitive behavioral therapy, behavioral intervention and education intervention strategies, but there is insufficient evidence of existing nurse-involved intervention strategies for medication compliance of kidney transplantation patients, and the selection of the best intervention strategy is difficult and complex. High-quality, large-sample studies are still needed in the future.

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312.2

National <35YEARS-Split Liver Policy Improved Children's Access to Transplant in Spain

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Introduction: Children’s access to liver transplant in Spain was significantly lower compared to adults because only pediatric donors, which are very scarce, were offered for pediatric recipients. This inequity was historically compensated by the extended use of living donation. In 2019, the Organización Nacional de Trasplante (ONT) established a new allocation policy to promote split liver donation in young brain death donors.

Aim: To analyze the impact of the new <35years-split policy on the pediatric waiting list and the need of living donation.

Material and methods: The <35y-split policy established that all donors were offered to pediatric groups for consideration of split liver donation. The data from the ONT registry corresponding to 2018 and 2021 were compared. The period of 2019-2020 was excluded because of the pandemic and the possible interference of the transitional period.

Results: After the <35years-split policy implementation, the pediatric waiting list showed a 60% reduction (32 vs 14 active patients). Pediatric transplant probability was significantly improved (38% vs 73%, p<0.05), while the probability in adults remained stable (68% vs 65%). Time on the waiting list also improved in children (72 vs 27 days, p<0.05) with a minor impact in adults (48 vs 69 days, p=ns). Children’s Mortality on the waiting list experienced a 40% reduction. The need of living donation dramatically reduced (20/y vs 1/y, p<0.05).

Conclusions: The introduction of the <35years-split policy by the ONT significantly improved the access of the pediatric population to liver transplant without a negative impact on the adult waiting list. The use of living donor was reserved to selected cases although not completely eliminated.

312.3

Outcomes of Duct-To-Duct Biliary Anastomosis in Pediatric Liver Transplantation Using Left Sided Graft

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Background: Roux-en-Y hepaticojejunostomy (HJ) is the standard-of-care for biliary reconstruction in pediatric liver transplantation (LT) with a higher hilar dissection and patch anastomosis technique under a prospective protocol. (Figure 1) The exclusion criteria were: 1) disease mandated HJ, 2) widely separated graft bile ducts that ductoplasty was infeasible, 3) native biliary anatomical factors that rendered a patch infeasible. Size discrepancy was not a contraindication. The primary endpoint was the risk of biliary complication. LT survival rates was 98.2% and 96.8% respectively.

Conclusion: DDA was safe and feasible with excellent perioperative and long-term outcomes and should be considered the primary choice for biliary reconstruction in eligible pediatric transplant patients.
Abstracts

312.4

Surgical Management of Portal Venous Thrombosis in Patients Undergoing Liver Transplantation Proposed of an Algorithm

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Introduction: Portal vein thrombosis (PVT) is common in patients with liver cirrhosis, undergoing liver transplantation (LT); in our environment, this is the first publication with an emphasis on results and surgical strategies.

Objectives: It was to review the casuistry of the Guillermo Almenara Irigoyen National Hospital, determine characteristics, types of PVT and surgical management.

Materials and Methods: The medical records of cirrhotic patients undergoing LT who presented PVT between March 2000 and June 2021 were analyzed. During this period, 304 liver transplants were performed in 285 patients, 256 adults and 29 pediatric patients; the latter were excluded.

Results: We found 46 patients with PVT (17.9%), diagnosed before and during LT, none of malignant aetiology; the most frequent etiologies of cirrhosis were non-alcoholic steatohepatitis (37.4%), alcoholic steatohepatitis (22%), autoimmune hepatitis (AIH) (11%), hepatitis B virus (HBV) (7.4%) and others (11.5%). According to the Yerdel Classification, we find: Grade I: 22 (48%), Grade II: 15 (32.5%), Grade III: 6 (13%) and Grade IV: 3 (6.5%). The surgical strategies used were: thrombectomy in 40 (87.1%); Cavoportal hemitransposition in 2 (4.3%), reno-portal anastomosis with vein graft interposition in 2 (4.3%) and thrombovenectomy plus vein graft interposition in 2 (4.3%). In 3 cases there were re-PVTs (6.5%). We observed that PVT decreased patient survival after LT: One year (81.2%), 3 years (78.4%) and 5 years (78.4%) compared to patients without PVT at 1 year (84.6%) 3 years (82.3%) and 5 years (82.3%).

Conclusion: Cirrhotic patients with PVT were clinically more decompensated, survival decreased with a higher degree of PVT. Surgical conduct was similar to other transplant centers; early diagnosis was essential to take an early surgical approach and reduce morbidity and mortality after liver transplantation. A management algorithm for portal vein thrombosis before liver transplantation is proposed.

Key words: Portal Vein Thrombosis, Liver Transplantation, Yerdel Classification, Surgical Strategy.

Table 1. Pre-transplant characteristics of all patients who had duct-to-duct biliary anastomosis.

<table>
<thead>
<tr>
<th>Age, months (range)</th>
<th>30.5 (3-200)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N, % male</td>
<td>63 (57.3%)</td>
</tr>
<tr>
<td>Diagnosis (n, %)</td>
<td></td>
</tr>
<tr>
<td>Acute liver failure</td>
<td>4 (3.6%)</td>
</tr>
<tr>
<td>Metabolic disease</td>
<td>89 (80.9%)</td>
</tr>
<tr>
<td>Hepatoblastoma</td>
<td>4 (3.6%)</td>
</tr>
<tr>
<td>Cholestatic liver disease</td>
<td>4 (3.6%)</td>
</tr>
<tr>
<td>Others</td>
<td>9 (8.2%)</td>
</tr>
<tr>
<td>Body weight, kg (range)</td>
<td>12.75 (5-3.47)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Graft type (n, %)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Left lateral section graft from living donor</td>
<td>86 (78.2%)</td>
</tr>
<tr>
<td>Left lobe from living donor</td>
<td>12 (10.9%)</td>
</tr>
<tr>
<td>Left lateral section graft from split donor</td>
<td>11 (10.0%)</td>
</tr>
<tr>
<td>Left lobe from split donor</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Number of graft bile duct (n, %)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>104 (94.5%)</td>
</tr>
<tr>
<td>2</td>
<td>5 (4.5%)</td>
</tr>
<tr>
<td>3 or more</td>
<td>1 (0.9%)</td>
</tr>
</tbody>
</table>
Normothermic Machine Perfusion (NMP) Improves Access To Transplantation for Late Liver Re-Transplant Candidates

Dimitri Sneiders1, Hanns Lembach1, Angus Hann1, Anisa Nufut1, James Hodson2, John Isaac1, Rhiannon Taylor2, Matthew Armstrong1, Thamara Perera1, Hermien Hartog1.
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Introduction: Late liver re-transplantation (LLrT) is a complex surgical procedure. Candidates for LLrT spend longer on the waitlist than primary transplant candidates due to selectivity in accepting organ offers. A service design using NMP was implemented in October 2018 at a single centre to facilitate increased organ utilisation of marginal organs for high-risk recipients. The aim of this study was to assess if this intervention improved access to transplantation.

Methods: Adult patients electively listed between 2015 and 2020 for LLrT were identified from the national transplant authority database. Transplant rates prior to (period 1) and after (period 2) local implementation of the NMP service design (October 2018) were compared at the study centre and compared to the collective data from other UK centres. A cause-specific Cox regression model was used, with the period modelled as a time-dependent covariate, and the period*centre interaction being the primary factor of interest. The model was corrected for UKELD, age, indication, and blood type. Post-transplant graft survival was assessed with univariable cox regression.

Results: A total of 144 and 338 LLrT candidates were listed in the study and control centres respectively. At the study centre, the likelihood of transplantation within one year of listing increased from 56% to 68%, whilst a reduction in the LLrT rate was observed at other centres (Figure). Multivariable analysis showed improved transplant access at the study centre in period 2 (period*centre interaction: HR: 1.83, 95%CI: 1.15-2.9, p=0.01). Post-transplant graft survival was not affected by the intervention (HR: 1.06, 95%CI: 0.41-2.69, p=0.903).

Discussion: Implementation of the NMP service design significantly improved access to transplantation for LLrT candidates, without compromising graft survival. While organ utilisation benefit for NMP has been demonstrated before, this is a first study showing a direct patient benefit of NMP for patients with long expected waiting times.

Results of multivariable cause specific cox regression (timepoint transplantation)

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood type</td>
<td>0.61 (0.32-0.86)</td>
<td>0.001</td>
</tr>
<tr>
<td>D</td>
<td>0.76 (0.35-1.64)</td>
<td>0.190</td>
</tr>
<tr>
<td>E</td>
<td>1.45 (0.72-2.94)</td>
<td>0.311</td>
</tr>
<tr>
<td>UKELD at listing</td>
<td>1.00 (0.79-1.25)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at listing</td>
<td>1.01 (0.96-1.06)</td>
<td>0.952</td>
</tr>
<tr>
<td>Hepatitis A/B/C</td>
<td>1.19 (0.97-1.48)</td>
<td>0.175</td>
</tr>
<tr>
<td>Period 1</td>
<td>reference</td>
<td></td>
</tr>
<tr>
<td>Period 2</td>
<td>0.86 (0.68-1.08)</td>
<td>0.159</td>
</tr>
<tr>
<td>Study centre</td>
<td>0.72 (0.51-1.05)</td>
<td>0.095</td>
</tr>
<tr>
<td>Period 2 in study centre (period*period interaction)</td>
<td>1.04 (1.03-1.05)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Results are from a cause specific Cox regression model, with transplantation being the event of interest. The period was treated as a time-dependent covariate. The interaction term represents a comparison of change from period 1 and period 2 between the two groups of centers.

Figures:

Fig. 1. Imágenes de angiotomografía con reconstrucción vascular en nuestros pacientes donde se puede observar los tipos de TVP de acuerdo a la Clasificación de Yerdell. A. Grado 1, <50% de trombosis de la luz del vaso con o sin extensión hacia la vena mesentérica superior (VMS); B. Grado 2, trombosis 2-50% de la luz del vaso u oclusión total del vaso con o sin extensión de la vena mesentérica superior; C. Grado 3, trombosis venosa portal completa y trombosis proximal de la vena mesentérica superior; D. Grado 4, trombosis venosa portal completa con extensión distal de la vena mesentérica superior.

Fig. 2. Trasplante de Hígado en paciente cirúrgico con TVP de acuerdo a la clasificación Yerdell IV, en la imagen A. Se aprecia el momento posterior a la reperfusion, se ve el hilo del injerto hepático donde se evidencia la vena porta (flecha azul), la interposición del injerto vascular de vena ilíaca entre la vena porta y la vena renal izquierda y abordada por espacio retroperitoneal (flecha amarilla), además se puede observar arteria hepática con conducto arterial proveniente de la aorta infrarenal (flecha roja). Imagen B. Se aprecia la angiotomografía con reconstrucción vascular posterior al trasplante.
312.6 Model for Virtual Vascular Reconstruction in Liver Transplantation Using Computational Fluid Dynamics

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Introduction: Computational anatomy is a modern research method that has become available using computer technology and computational fluid dynamics. It is promising to use it for perioperative planning and modeling, including organ transplantation. Aim of study is to prepare investigational model of blood flow in liver during liver transplantation.

Materials and methods: Contrast research was done among 53 men who were patients in surgery departments at Krasnoyarsk regional hospital #1, Russia (KRH). Estimations were made using 3D models of portal system (working stations GE Advantage Workstation, Siemens singo.via), based on multi-slices computed tomography of abdominal cavity with bolus contrast-ing with help of medication “Ultravist-370”. The volume of the used contrasting stuff made 100 ml, the speed of infiltration was 4 ml per second, and the average radial strain was 11,3 m3v. DICOM data segmentation was performed using Dragonfly software (Object Research Systems, Canada) at the Innovation Technology Management Resources of the Reaviz University. Using series with arterial and vein contrast, we performed the segmentation of contrasting vessels, and obtained three-dimensional data topology in.obj format. Then we processed the obtained models using scripts prepared for the pythonOCC framework. We built the central lines of the vessels and formed the branching tree. Methods of computational hemodynamics were implemented using the Visual-CFD application for OpenFOAM environment (ESI, France). Mesh example of portal vein shown in figure 1.

Results: With the use of created three-dimensional computer model, the blood flow in the portal vein and liver arteries at various variants of its structure was simulated. It was obtained that, in the presence of the main type of structure with predominance of blood flow along the splenic vein, the blood flow turbulence and risk of thrombosis development are higher. At the same time, with virtual thrombosis of the portal vein trunk, the pressure gradient is 1.4 times higher than with the bulk type, which is more favorable for the proposed reconstruction. Thus, these data can be used for preoperative planning in surgical treatment of portal vein thrombosis in liver transplantation.

Conclusion: The proposed model of blood flow is promising and allows you to create an interactive tool for calculating the hemodynamic situation in various reconstructions during liver transplantation.

312.7 Liver Transplantation in a Complex Recipient Anatomy.

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A 22-year-old man with situs inversus totalis and end-stage liver disease secondary to congenital biliary atresia and previous Kasai portoenterostomy at two months who was referred to our center with portal hypertensive bleeding, recurrent cholangitis, and hepatocellular carcinoma. He completed the liver transplant protocol. Preoperative liver angiotomography revealed, besides the mirror image orientation of the viscera and dextrocardia, inferior vena cava (IVC) and portal vein (PV) with good patency, splenorenal shunt, collateral circulation, and common hepatic artery arising from the superior mesenteric artery. A suitable 59-year-old cadaveric male donor with no anatomic variation was accepted. He underwent to liver transplant, his BMI was 16.7kg/m2, MELD and Child-Pugh scores were 24 and 7 points. The donor’s liver weighed 1725g.

A bilateral subcostal incision was made; after extensive lysis of adhesions, the hepatectomy was performed with preservation of the recipient’s IVC. The donor’s liver was placed on the left side rotated 90° clockwise; this allowed perfect alignment of the recipient and dolor hila. The donor infra-hepatic vena cava was anastomosed end-to-side to recipient IVC previous closing of the suprahepatic vena cava. The artery and PV were anastomosed end-to-end without vessel grafts. A choledochojejunostomy was performed using the previous Roux-en-Y. The patient had satisfactory evolution and was discharged on the 8th postoperative day with normal liver function.
What Is the Risk Factor of Graft Mortality in Patients Who Underwent Simultaneous Splenectomy During Living Donor Liver Transplantation?

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Introduction: Splenectomy is performed in living donor liver transplantation (LDLT) for portal flow modulation. The aim of this study was to identify the risk factor of 6-month graft mortality in patients who underwent splenectomy in LDLT.

Methods: Data from 441 adult patients who underwent simultaneous splenectomy during primary LDLT were collected retrospectively. Risk factors of 6-month graft mortality were investigated.

Results: Mean recipient age was 55 years. Mean donor age was 38.7 years. Two hundred and five patients (46.5%) received left lobe graft. Mean graft weight (GW)-standard liver weight ratio was 41.5% and GW-recipient weight ratio was 0.79%. Six-month graft survival rate after LDLT in 441 patients was 93.8%, which was significantly better compared to patients without simultaneous splenectomy or splenic artery ligation (83.9%, p<0.0001). Univariate analysis revealed the following risk factors for 6-month graft mortality in patients with splenectomy: neutrophil-lymphocyte ratio > 4, acute liver failure, hospitalized before LDLT, donor > 60 years of age, MELD score > 22, pre-LDLT platelet < 40,000/mm3, portal vein pressure when LDLT finished (PVP) > 20 mmHg. Multivariate analysis identified that donor > 60 years of age (Hazard ratio=4.50, p=0.049), pre-LDLT platelet < 40,000/mm3 (Hazard ratio=2.58, p=0.03), and PVP > 20 mmHg (Hazard ratio=7.46, p<0.001) were the independent risk factors of 6-month graft mortality after LDLT.

Conclusion: Splenectomy in LDLT improves survival rate after LDLT. Careful attention is needed for patients with platelet < 40,000/mm3, PVP > 20 mmHg, and received graft from donor > 60 years of age.
Abstracts

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Mathematical Modelling to Determine Segment Perfusion Parameters for Living Donor Liver Transplantation

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Introduction: Adult-to-Adult Living Donor Liver Transplantation (A2ALL-1) Cohort Study focused on hepatic blood flow and effect of portal modulation in smaller and left lobe grafts demonstrating a significantly (p = 0.03) higher graft dysfunction in modulated recipients versus unmodulated. The study concluded the need for prespecified portal flow and hepatic venous outflow modulation protocols to better define outcomes of volumetric interventions. We developed a mathematical model of the liver to determine hemodynamic parameters across segments following simulated liver resections and middle hepatic vein interventions in both the remnant donor liver and recipient grafts to predict functional graft outcomes prior to reperfusion.

Methods: Arterial/portal/hepatic vein and terminal portal triad diameters from 12 deceased donor livers and biopsies were used in a custom lumped parameter model developed in MATLAB {Fig(a)}. Blood flow is modeled using the Hagen-Poiseuille equation, and the continuity equation is solved to obtain volume flow rate of the whole liver at every point throughout the network {Fig(b)}. Simulated right hepatectomy in the plane of resection shown in Fig(a) is used to derive variations in blood flow and volume through the modeled left liver lobe {Fig(c)}.

Results: Schematic illustrations of the modeling components of liver segments demonstrate volume flow rate encoded in pseudocolor mapping in the donor liver before and after right heptatectomy (Fig(b)). Localized increase in blood flow through 2nd and 3rd generations of vessel division is especially apparent in the donor’s simulated remnant left lobe {Fig(c)}. Volume and flow rate alterations in hepatic venous outflow following ligation/reconstruction of middle hepatic veins in the remnant left lobe is evident. Perfusion parameters in the donor graft are also captured to simulate graft perfusion prior to reperfusion in the recipient.

Conclusion: Surgical intervention on the middle hepatic vein (MHV) is critical for donor remnant liver outflow and optimal perfusion in the donor graft. Mathematical simulations to predict hemodynamic inflow – outflow parameters in living donor liver transplantation could help guide MHV ligation and reconstruction as well as predict graft perfusion parameters prior to reperfusion.

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Risk factors of graft loss within 6-month after LDLT

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>NLR &gt; 4: Yes vs. No</td>
<td>2.91</td>
<td>1.35 – 6.26</td>
</tr>
<tr>
<td>ALF: Yes vs. No</td>
<td>3.80</td>
<td>1.31 – 11.0</td>
</tr>
<tr>
<td>Hospitalized: Yes vs. No</td>
<td>5.08</td>
<td>2.22 – 11.6</td>
</tr>
<tr>
<td>Age ≥ 60: Yes vs. No</td>
<td>1.04</td>
<td>0.48 – 2.28</td>
</tr>
<tr>
<td>Male: Yes vs. No</td>
<td>1.89</td>
<td>0.88 – 4.07</td>
</tr>
<tr>
<td>Donor age ≥ 80: Yes vs. No</td>
<td>4.75</td>
<td>1.43 – 15.8</td>
</tr>
<tr>
<td>Donor Male: Yes vs. No</td>
<td>1.05</td>
<td>0.49 – 2.25</td>
</tr>
<tr>
<td>Right lobe graft: Yes vs. No</td>
<td>0.88</td>
<td>0.41 – 1.88</td>
</tr>
<tr>
<td>GWR/LWR ≥ 35%: No vs. Yes</td>
<td>0.54</td>
<td>0.19 – 1.56</td>
</tr>
<tr>
<td>Portal pressure at the end of LDLT: No vs. Yes</td>
<td>7.54</td>
<td>3.26 – 17.0</td>
</tr>
<tr>
<td>Pre-LDLT platelets &lt; 400 x 10^9 /mL: Yes vs. No</td>
<td>2.26</td>
<td>1.05 – 4.86</td>
</tr>
<tr>
<td>MELD ≥ 22: Yes vs. No</td>
<td>3.77</td>
<td>1.77 – 8.02</td>
</tr>
<tr>
<td>Portal vein stenosis: No vs. Yes</td>
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Use of Transient Liver Elastography in the Evaluation of Liver Viability for Organ Donation and Transplantation

Ernesto Duarte-Tagles1,2, Martha Susana Pérez-Cornejo1,2, Luis Carlos Rodríguez-Sanch2, Jorge Rubén Béjar-Cornejo1, Mario Alberto Flores-León1,2, Alejandro Lugo-Barquín2, Salvador Castillo-Barón2, Marisela Corea-Valdez2, José Armando Portugal-Lazcano1,2.
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Introduction: The lack of enough livers for transplant worldwide is a reality and in México because of donation rates and high prevalence of morbid obesity this condition is worse. Strategies to determine whether a liver is suitable for donation depends on many occasions on the predonation estimation of fatty content. For March 2022, exist 244 patients in waiting list for liver transplant. In 2021 only 135 transplants were performed out of 293 brain death donors (none non heart beating donors). The reasons why 53.9% of the livers are not use are wide but one of them is because the higher prevalence of overweight and obesity in Mexican population, meaning a high number of steatosis of the liver. Since there is also a poor air connectivity among Mexican cities, the risk for primary organ failure is increased by longer ischemia time. Because the common study to evaluate liver steatosis is ultrasound despite the poor sensitivity, we proposed to use Transient elastography as a bedside tool to evaluate fat content or fibrosis of the liver condition before harvesting, minimizing the mobilization of complex and expensive logistics necessary to harvest a liver just to be discarded later and assuring better transplant results.

Method: A prospective double-blind study was conducted in Hospital General del Estado from October 2015 to November 2021 that consist in that in every donor, no matter body mass index, a liver ultrasound was made by a radiologist and later a liver elastography was made on the same donor by another radiologist. Then the results were confronted during the organ harvesting by surgeon expertise who decided to take liver or not.

Results: We had 32 brain death organ donors to whom an ultrasound and liver elastography was made. Median age was 41 years and weight were 74.66 kgs, with a range from 55 to 120 kgs. By using conventional ultrasound, out of the 32 donors, 93.8% were diagnosed without liver steatosis and 3.1% with mild and 3.1% with severe, while elastography showed 50% no steatosis, 15.6 light, 6.3 mild and 28.1 severe. Correlation of Transient elastography with surgical appearance was 100 % (No biopsy was taken to correlate this results with pathology).

Conclusion: Our study showed that using ultrasound for evaluate liver steatosis for organ donation is not as good as it might be thought. For no liver steatosis concordance between ultrasound and elastography was 50% but in cases for severe infiltration, diagnosed rate was 1 Vs 9 for ultrasound vs elastography, and severe steatosis confirmed at the moment of surgery being evident the superiority of elastography for diagnosis of mild to severe steatosis and becoming a better resource in the evaluation of brain death organ donor.
Higher Tomographic Abdominal Fat Volume Is Associated With Lower Renal Function Before and Long-term After Living Kidney Donation

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Introduction: Central body fat distribution, in which most fat is accumulated in the abdominal region, has been associated with increased risk of renal function impairment. Especially an excess of visceral fat is accompanied by an increased renal risk. Although body mass index (BMI) is facing increasing scrutiny due to its inability to accurately assess body composition, it remains the gold standard in screening guidelines for living kidney donation. Abdominal fat measurements using computed tomography (CT) may prove superior in assessing body composition related renal risk for living kidney donors. This study aimed to identify donors with high levels of total abdominal, visceral, subcutaneous or intramuscular adipose tissue (TAT, VAT, SAT, and IMAT, respectively) and determine the association with renal function before and (long term) after donor nephrectomy. Potential differences between CT-derived fat measurements and BMI, as a measure of body composition-related post-donation renal risk, were investigated.

Methods: Between 2002 and 2019, 970 living kidney donors from the University Medical Center Groningen were included in this study. Volumes of abdominal fat compartments were determined from an axial CT slice at vertebral level L3. Donors underwent glomerular filtration rate measurements (mGFR (125I-Iothalamate)) prior to donation and at 3 months, 5 and 10 years after donation. Uni- and multivariable linear regression analyses were performed to assess the association of tomographic fat measurements and BMI with renal function.

Results: Mean donor age was 53 ± 11 years and 50% were male. Multivariable linear regression analyses in both male and female donors showed that higher levels of TAT, VAT, SAT, and IMAT were all significantly associated with lower mGFR levels at screening for donation (male donors: TAT: B=-0.06, p<0.001; VAT: B=-0.04, p=0.002; SAT: B=-0.06, p=0.004, and IMAT: B=-0.36, p=0.01; female donors: TAT: B=-0.07, p=0.001; VAT: B=-0.06, p<0.001; SAT: B=-0.07, p<0.001, and IMAT: B=-0.32, p<0.01). In contrast, higher BMI was significantly associated with higher mGFR at screening (male donors: B=1.35, p<0.001; female donors: B=1.09, p<0.001). Long-term after donation, tomographic abdominal fat measurements remained inversely associated with mGFR in male donors. For female donors, this was only the case at 3 months after donation. Higher BMI remained associated with higher mGFR levels long-term after donation in both male and female donors.

Conclusion: This study shows that abdominal fat volume has a negative effect on renal function at time of screening and (in male donors) long-term after living kidney donation. In contrast, BMI was associated with higher mGFR levels during screening and long-term after donation. Comprehending the renal outcomes of living kidney donation and accurately identifying their body composition related risk factors can aid clinicians in decision-making and donor counseling during screening for donation.

Domino Kidney Transplant Following Nephrectomy for Renal Artery Stenosis With Arterial Reconstruction and Viability Assessment Using Ex Vivo Normothermic Perfusion: A Case Series

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Introduction: Ex vivo normothermic perfusion (EVNP) is increasingly recognised as a viability tool to increase organ utilisation. We report use of EVNP to assess graft perfusion of potential domino transplants following therapeutic nephrectomy and backbench arterial reconstruction in four cases of refractory hypertension secondary to renal artery stenosis (RAS) unsuitable for endovascular treatment.

Case Detail: Patient A and Patient B had isolated unilateral RAS presumed secondary to fibromuscular dysplasia. Pre-operative imaging and functional assessment revealed a split function of the affected kidneys to be 38% and 43%, for Patient A and Patient B, respectively. Patient C and Patient D had a wider distribution of vascular occlusive disease. Patient C had an occluded left renal artery with an atrophic left kidney and no evidence of function on isotope imaging. Following unsuccessful angioplasty and stenting, Patient D had developed in stent occlusion; subsequent imaging demonstrated hypoperfused right kidney with 6% estimated split function.

Outcome: Following nephrectomy, all kidneys were prepared on the back-bench for EVNP. For Patient A and Patient B, a common stem was created using spatiulation of the renal artery and reconstruction with collateral vessels (plus saphenous vein patch in Patient B). Both grafts perfused well with excellent global perfusion and urine output (EVNP assessment score=1). Beyond the stent stenosis, the renal artery from Patient C was short but allowed cannulation following dilatation. Patient D required separate cannulation (to renal artery and main collateral) with 14G cannula. Patient C and Patient D demonstrated high resistance and poorer perfusion (EVNP assessment score=4). The kidneys from Patient A and Patient B were successfully transplanted into two dialysis-dependent patients who achieved primary function and eGFR of 58 and 62ml/min/1.73m2, respectively.

Discussion: The demonstration of adequate arterial reconstruction plus excellent graft perfusion whilst on EVNP, alongside favourable pre-operative functional imaging, provided confidence to transplant two marginal domino grafts.
Evaluating Telehealth as a Means of Communicating With Living Donors and Its Effects on Quality of Care

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1George Washington University, Washington, DC, United States; 2Transplant, MedStar Georgetown University Hospital, Washington, DC, United States.

Purpose: Telemedicine has allowed MedStar Georgetown Transplant Institute (MGTI) to connect safely with our donors during the COVID-19 pandemic, but it has also highlighted the positive impact telehealth can have on addressing barriers to kidney donation including time/distance to the transplant center and out-of-pocket costs related to travel and time off work. Nonetheless, prospective evaluation is needed to determine whether reliance on telehealth affects quality of care compared to in-person evaluations including, access to care, effectiveness, financial impact, and experience.

Methods: Utilizing a pretest-posttest design, an analysis was performed among medically cleared donors evaluated in-person between 1/1/2019 to 12/31/2019 (Control Group; N=64) and donors evaluated via telehealth between 1/1/2021 to 12/31/2021 (Intervention Group; N=64). Mean outcome measures included referral date to evaluation date (access to care); evaluation date to medical clearance date (effectiveness); and estimated out-of-pocket costs related to travel and lost wages (financial impact). Telehealth Usability Questionnaires (TUQ) were used to evaluate healthcare provider/patient experience.

Results: Donors evaluated via telehealth were scheduled for an evaluation significantly faster than in-person evaluations (51 days vs 30 days). The total estimated financial impact for donors completing telehealth evaluations was significantly lower than in-person evaluations ($1029 vs $1875). Also, telehealth donors faced lower out-of-pocket costs related to lost wages ($2,174 vs $3,400).

Discussion: Results align with published research which show telehealth may improve access to care and alleviate financial burden, making living donation more accessible and convenient. Donors evaluated via telehealth were scheduled for their evaluation 21 days faster and faced $846 less in out-of-pocket expenses related to travel and lost wages. In addition, donors and health care providers were all highly satisfied with their telehealth experience, with the majority finding it to be equivalent to a traditional in-person visit, with quality and convenience driving this ranking.

Recommendations: Using telehealth for living donor evaluations and care after donation has the ability to transform the healthcare delivery system by helping to overcome geographical distance, enhancing access to care, and reduce financial barriers to donation. However, telehealth evaluations should not be seen as a complete replacement for in-person evaluations which are better suited for donors with complicated surgical history, language barriers, or with-out high-speed internet access, etc. Collaborative efforts to advance regulatory policies, develop best practices, and alleviate licensure restrictions are vital for continued access to telehealth for living kidney donor evaluation and care.

Matthew Cooper, MD Jennifer Verbesey, MD Gayle Vranic, MD.
Abstracts

313.5

Meeting Packed Red Blood Cell Requirement for the Transmedics Organ Care System (OCS) Liver Transplantation Trial (PROTECT Trial) At Henry Ford Hospital

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Introduction: In January 2016, HFHS Transplant Institute began the PROSPECT trial, an interventional trial studying normothermic preservation of the donated liver before transplant using the Liver Organ Care System (OCSTM). The Henry Ford Hospital Transfusion Service (TS) provided the required packed red blood cells (PRBC).

Background: The TransMedics (OCSTM) liver trial was an international, randomized trial studying the intervention of a portable liver system to preserve donor livers for transplant. The system utilizes an oxygenated blood-based perfusate mixed with nutrient solution in normothermic perfusion for organ preservation. The TS provided PRBC needed for the study, final PRBC used dictated by the condition and size of the retrieved liver. TS study goal was to secure proper transfusion needs for liver perfusion while also adhering to blood inventory management.

Methods: Organ procurement candidates for the PROTECT trial were selected based on pre-determined conditions and consented according to that protocol. Once the patient was consented and the liver transplantation was scheduled, the PROTECT trial team notified the TS, and 5 units of group O Positive, leukoreduced PRBC less than 10 days old were selected, and placed inside a temperature-controlled packaging container along with a remote temperature monitoring device. The container was then transported with the procurement team to the harvesting location. Once the insulated container was returned to the TS, the temperature-monitoring device information was uploaded to verify that the returned PRBC have been stored within their proper temperature limits.

Results: The TS support for the PROTECT trial at HFHS occurred from January 2016 until September 2021. The table below shows the activity related to this trial.

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Conclusions:

During the PROTECT trial no PRBCs were wasted due to inappropriate storage conditions. The joint use of a temperature-controlled container and remote temperature monitoring device allowed for the appropriate return of unused PRBCs to the TS blood inventory, thus avoiding any wastage. Only 3/48 events used 5 units; the remaining 4 PRBC were spiked in preparation for use in the perfusate prior to the event being cancelled. These PRBC were discarded and deemed wasted.

Conclusions: During the PROTECT trial no PRBCs were wasted due to inappropriate storage conditions. The joint use of a temperature-controlled container and remote temperature monitoring device allowed for the appropriate return of unused PRBCs to the TS blood inventory, thus avoiding any wastage. Only 3/48 events used 5 units; the remaining 4 PRBC were spiked in preparation for use in the perfusate prior to the event being cancelled. These PRBC were discarded and deemed wasted.

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<table>
<thead>
<tr>
<th>PRBC units</th>
<th>Issued</th>
<th>Utilized</th>
<th>Returned</th>
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Early Graft Dysfunction After Hypothermic Oxygenated Machine Perfusion of ECD Criteria Liver Grafts: No Longer A Clinical Issue?

Florin Botea1, Alexandru Barcu1, Cosmin Verdea1, Radu Zamfir1, Doina Hrehoreț1, Dana Tomescu1, Vlad Herlea1, Vladislav Brasoveanu1, Irinel Popescu1.
1Dan Setlacec” Center of General Surgery and Liver Transplantation, Fundeni Clinical Institute, Bucharest, Romania.

Introduction: Early allograft dysfunction (EAD) continues to be an important issue in liver transplantation, varying from 15 to 30%. This rate is particularly high in case of extended criteria donor (ECD) grafts due to significant ischemia-reperfusion injury leading to EAD. This injury is substantially reduced by thermoregulated oxygenated machine perfusion. The aim of the paper was to assess the use of hypothermic oxygenated machine perfusion (HOPE) in ECD liver grafts in a high-volume liver transplantation center using a specific protocol.

Method: Grafts with >30% macrosteatosis and with multiple ECD (at least 2 criteria) were perfused using dual HOPE (hepatic artery and portal vein perfusion), while HOPE (portal vein perfusion only) was used for the remaining ECD grafts. The main criteria to establish graft improvement were the improvement of arterial and portal perfusion flows, with lactate under 3 mmol/L throughout the procedure.

Results: Between February 2016 and February 2022, 26 ECD liver grafts were harvested from DBD (donation after brain death) donors and benefitted from HOPE. Dual HOPE was used in 8 grafts (30.7%). Criteria for graft improvement were met in all grafts except 5 (19.2%), where lactate was over 3 mmol/L, with a median of 3.6 (range 3.5–6.1). The median follow-up was 5 months (range 2–44). No EAD was encountered.

Conclusion: By using a combined protocol of HOPE and dual HOPE, ECD liver grafts may be safely used by avoiding early graft dysfunction.

Hypothermic Machine Perfusion Ameliorates Fibrinolysis And Microthrombi Clearance After DCD Kidney Donation

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1Department of Surgery, University Medical Center Groningen, Groningen, Netherlands; 2Surgical Research Laboratory, Department of Surgery, University Medical Center Groningen, Groningen, Netherlands; 3Department of Pathology, University Medical Center Groningen, Groningen, Netherlands; 4Division of Nephrology - Department of Internal Medicine, University Medical Center Groningen, Groningen, Netherlands.

Oxygenated hypothermic machine perfusion (HMP) is superior to static cold storage (SCS) in kidney transplantation. However, the mechanisms determining this superiority have only been studied to a limited extent. The aim of this study was to investigate whether HMP is superior because it provides a prolonged and better flush, removing microthrombi and fibrin depositions that may have accumulated in the kidney after circulatory arrest. Viable porcine kidneys from an abattoir underwent 35 minutes of warm ischemia, were flushed with 500mL heparinized cold University of Wisconsin solution and subsequently preserved for 3.5 hours using either SCS, HMP, or HMP+alteplase (HMP+) (Figure 1). D-dimer, von Willebrand factor (VWF) and tissue-type plasminogen activator (tPA) levels were measured in perfusate samples at set times. The first and last perfusate sample prior to and after SCS/HMP was taken from a separate 50mL flush, directly from the renal vein. Kidney punch biopsies were immunohistochemically stained for an antibody against fibrinogen. Warm and cold ischemic times were comparable between groups. The median [IQR] duration of the flush was 11 min [6–15] in SCS, 9 min [7–12] in HMP and 9.5min [7–11] in HMP+. There was no significant difference between total VWF release into the perfusate between groups after storage (SCS 1.65 ug [1.28–3.30] vs. HMP 1.87 [1.11–4.00] vs. HMP+ 1.70 [1.11–3.06] p=0.80, Figure 2). However, total D-dimer release was much higher in the HMP and HMP+ groups compared to SCS (24,650 ng [2,380–38,164] and 25,840 [9,010–45,050] ng vs. 6,325 [2,100–7,550], p=0.09 and p<0.01, respectively). In SCS treated kidneys there was a small increase in microthrombi over time (0.30 microthrombi/mm2 [0.22–1.39] to 0.73 [0.22–1.08]), while there was a decrease in the number of microthrombi in HMP- (0.91 [0.07–2.30] to 0.57 [0.19–1.34]) and HMP+ (0.63 [0.43–1.24] to 0.34 [0–0.87]) preserved kidneys. Our results suggest that the superiority of oxygenated HMP is at least partly caused by a better flush to clear the kidney graft from donor-derived thrombi, considering an increased release of D-dimer, and a reduction of microthrombi over time. This phenomenon has already been observed in machine-perfused human livers. Furthermore, HMP does not significantly increase endothelial activation, as evidenced by low levels of VWF in the perfusate. Addition of a thrombolytic agent to an HMP-fluid does not seem to be of added value.
One OPO’s Experience With Normothermic Regional Perfusion

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1Clinical Services, Southwest Transplant Alliance, Dallas, TX, United States.

Introduction: The ability to increase the organ yield from Donation after Circulatory Death (DCD) donors is an urgent need. There have been advances in the ability to evaluate organs in a normothermic ex-vivo fashion, but the opportunity to perfuse and evaluate organs in-situ has been lacking. Normothermic Regional Perfusion (NRP) has provided transplant centers with the ability to assess organs on a DCD donor in similar fashion to the circumstances of Donation after Brain Death (DBD) procurement. This provides another option to increase the number of organs that are deemed suitable for transplantation.

Methods: We compared our traditional DCD donors (n=110) to our NRP DCD donors (n=9) from 1/01/2021-2/28/2022. We compiled data consisting of donor age, warm ischemic time (WIT), death pronouncement to NRP start, organs transplanted per donor, and recipient outcomes. From this data we determined averages and compared those to DCD recoveries completed without the use of NRP. We also compared recipient outcomes to DCD donors that utilized ex-vivo perfusion for the recovery and transplantation of the heart.

Results: Within our OPO, we define Warm Ischemic Time (WIT) as the start of the agonal phase (systolic BP < 80 mmHg or SpO2 < 80%) to NRP start. Warm ischemic time in NRP DCD patients includes both the agonal phase and time to initiation of artificial regional perfusion (averaging 7 minutes). Recipients from a DCD donor in which NRP was utilized had an average length of stay (LOS) of 6 days versus 13 days for traditional DCD. Compared to traditional DCD heart recoveries (average LOS 23 days with one patient expiring 42 days post-transplant), the NRP average length of stay was 11 days. NRP donors had a lower average age (33) to traditional DCD donors (49). Additionally, within the NRP DCD population, we saw a higher number of organs transplanted per donor (OTPD) by almost 1 organ with NRP DCD at 2.71 OTPD and traditional DCD at 1.88 OTPD. This is in spite of an increase in average WIT by 11 minutes for NRP donors.

Conclusion: NRP is a valid option for DCD recoveries and provides the accepting centers with an opportunity to evaluate the organs as they would in a DBD recovery. Utilizing NRP DCD allows for optimal utilization of donors which may in turn lead to acceptance of longer agonal phases and warm ischemic time if these results persist with larger study populations.
Perfusate IL-6 Levels During Liver NMP Might Be Predictive For Hemodynamic Response and Catecholamine Demand After Reperfusion in the Recipient

Annemarie Weissenbacher1, Simon Mathis2, Benno Cardini1, Christina Bogensperger1, Gabriel Putzer2, Lukas Gasteiger2, Thomas Resch1, Rupert Oberhuber1, Dietmar Öfner1, Tobias J Hell3, Judith Martini2, Stefan Schneeberger1.

1Department of Visceral, Transplant and Thoracic Surgery, Center of Operative Medicine, Medical University of Innsbruck, Innsbruck, Austria; 2Department of Anaesthesiology and Critical Care Medicine, Medical University of Innsbruck, Innsbuck, Austria; 3Department of Mathematics, Faculty of Mathematics, Computer Science and Physics, University of Innsbruck, Innsbruck, Austria.; OrganLife.

Introduction: Normothermic liver preservation (NMP) has become a clinical routine at several transplant centres. Reperfusion-syndrome occurs less often in recipients of NMP-livers compared to cold stored livers. We hypothesized that perfusate interleukin (IL)-6 during liver NMP correlate with recipient hemodynamics in the post-reperfusion period.

Method: Consecutive NMP-liver transplants at a single-centre were prospectively analysed. Perfusate samples were collected at 1 and 6 hours of NMP and at the end of perfusion and analysed for IL-6 levels. Median arterial pressure (MAP) and catecholamine need during surgery were recorded. The anhepatic phase was defined as baseline for MAP and catecholamine requirements.

Results: Over a period of 36 months, IL-6 perfusate measurements were assessed in 77 livers undergoing NMP and transplantation; 15/77 (19.5%) were DCD organs. The median donor age was 61 (15-87) years, median recipient age was 60 (19-73) years. Median (IQR) cold ischemia time was 6.2 (2.1) hrs, NMP-time and overall preservation time were 17.6 (10.4) hrs and 23.6 (10.6) hrs. Median (IQR) IL-6 levels (ng/L) after 1, 6 hrs and NMP-end were 52 (175), 278 (674) and 174 (2171). Neither duration of CIT nor NMP correlated with IL-6 levels over time. NMP-livers were stratified for the median of the last IL-6 measurement. Recipients receiving NMP-livers with perfusate IL-6 levels above the median developed significantly lower post-reperfusion MAP (dropping 20% from baseline) and displayed a significant higher demand of catecholamines (increase of 25% from baseline) up to 30 minutes after reperfusion. Perfusate IL-6 did not correlate with the occurrence of early allograft dysfunction.

Conclusion: Perfusate IL-6 levels during liver NMP are clinically relevant as they help to predict the post-reperfusion hemodynamics in recipients.
Single-Center Experience With “Extreme” Acute Kidney Injury Deceased Donor Kidneys

Alejandra Mena-Gutierrez1, Berjesh Sharda1, Matthew Garner1, Alan Farney1, Giuseppe Orlando1, Colleen Jay1, Amber Reeves-Daniel2, Natalia Sakhovskaya2, Robert Stratta1, Tim L Hamelink1, Merel B F Pool1, Rianne Schutter1, Cyril Moers3, Henri G D Leuvenink3, Rene A Poasma1, Leonie H Venema1

1Department of Surgery, Section of Transplantation, Atrium Health Wake Forest Baptist, Winston-Salem, NC, United States; 2Department of Internal Medicine, Section of Nephrology, Atrium Health Wake Forest Baptist, Winston-Salem, NC, United States.

Introduction: Although many centers will consider transplanting kidneys from deceased donors (DD) with mild acute kidney injury (AKI), a markedly elevated terminal serum creatinine (tSCr) level remains a major reason for kidney discard following organ recovery. The study purpose was to review retrospectively our experience with transplanting kidneys from “extreme” AKI (eAKI) DDs.

Methods: AKI kidneys were defined by a doubling of the DD’s admission SCr level and a tSCr level <2.0 mg/dl whereas eAKI kidneys were defined by a tSCr level ≥3.0 mg/dl. Dual kidney and multi-organ transplant recipients were excluded. All patients received depleting antibody induction and triple maintenance therapy (FK, MPA, steroids).

Results: From 1/07 to 11/21, we transplanted 236 single AKI kidneys including 100 from DDs with a tSCr level ≥3.0 mg/dl. 49 AKI DDs had a tSCr level ≥4.0 and the remaining 51 had a tSCr level between 3.0-3.9 (overall mean 4.2 mg/dl) in the eAKI group. Mean donor and recipient ages were 32.8 and 50 years, respectively. Mean KDPI was 44%. 62 patients (62%) had at least 5-year follow-up. This eAKI group was compared to 996 concurrent control patients receiving kidneys from DDs with a tSCr <1.0 mg/dl (mean donor and recipient ages 42.6 and 53 years, respectively; mean KDPI 54%, mean tSCr 0.7 mg/dl). The incidence of delayed graft function (DGF, dialysis in first week) was 51% eAKI vs 29% in controls (p=0.001) whereas the incidence of primary nonfunction (PNF) was 1% eAKI vs 2.6% controls (p=NS). One-year patient and kidney graft survival rates (GSR) were 98% vs 95% (p=NS) and 97% vs 91% (p=0.038) in the eAKI vs control groups, respectively. There were 2 early deaths in the eAKI group (respiratory failure at 3 months, cardiac event at 5 months) and the remaining early graft loss was secondary to PNF. With a mean follow-up of 79 months, overall patient and kidney GSRs were 84% vs 74% (p=0.029) and 71% vs 62% (p=0.038) in the eAKI vs control groups, respectively. Actual 5-year death-censored kidney GSRs were 85% eAKI vs 79% in controls (p=NS).

Conclusions: In spite of a higher incidence of DGF, patients receiving kidneys from DDs with tSCr levels ≥3.0 mg/dl have excellent medium-term outcomes compared to those receiving kidneys from DDs with tSCr levels <1.0 mg/dl. Although a selection bias may exist for AKI DDs (lower donor age and KDPI), a high tSCr level should not be considered a contraindication to transplantation.

Association of Hemoglobin Levels With Renal Metabolism and Function During Normothermic Machine Perfusion of Porcine Kidneys

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Introduction: Machine perfusion is widely studied as an opportunity to expand the kidney donor pool. Normothermic machine perfusion (NMP) of donor kidneys is increasingly implemented to preserve and assess renal function. However, the exact metabolic needs of an isolated perfused kidney are still unknown. Although all perfusion fluids are based on red blood cells or alternative oxygen carriers, hemoglobin levels are usually below physiological levels. It is unknown to which extent oxygen carrying capacity of hemoglobin is required to support kidney function during NMP. Therefore, the effect of hemoglobin levels on renal metabolism and function during NMP was retrospectively evaluated.

Methods: Using pooled data from our lab’s experimental work, slaughterhouse obtained porcine kidneys that underwent oxygenated NMP for four to six hours with a red blood cell-containing perfusion fluid between 2017 and 2022, were included in this study. All kidneys had a cold preservation period with either (oxygenated) hypothermic machine perfusion (HMP) or static cold storage (SCS). Kidneys were stratified according to arterial perfusate hemoglobin concentration at the start of NMP per 1 g/dl increment between 1,61/g/dl (= 1 mmol/L) and 12,89/g/dl (= 8 mmol/L). Outcome variables were fractional sodium excretion, creatinine clearance, oxygen consumption, lactate flux rates and adenosine triphosphate (ATP) levels during NMP.

Results: In total, 101 (75%) of 135 eligible kidneys were included. The mean hemoglobin level at the start of NMP was 8,17 g/dl (sd ±1,72 g/dl). A hemoglobin level ≥8,06 g/dl (= 5mmol/L) was associated with decreased fractional sodium excretion, indicative for improved tubular function. Moreover, oxygen consumption rates were higher and creatinine clearance appears to be higher in these groups as well. Other outcomes like lactate flux rates and ATP levels will be analyzed soon.

Conclusion: This preliminary study reveals that a minimum hemoglobin level of 8,17 g/dl (=5 mmol/L) may be important to support renal metabolism and function during NMP. Ultimately, these results can be translated to clinical NMP protocols.
Hypothermic Oxygenated Machine Perfusion of an En-Bloc Dual Kidney Specimen: Proof of Concept, in an Animal DCD Model, of a New Option to Preserve and Evaluate Kidney Grafts

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Introduction: Increasing use of donors after cardiac death (DCD) lead to a new interest in the organ perfusion. Sometimes in case of unavailability of multiple systems for organ perfusion or in case of contemporary multiple donors some organ could be statically cold stored instead than perfused possibly determining impaired function. Here we present an hypothermic oxygenated machine perfusion applied to an en-bloc dual kidney retrieved from an animal (pig) DCD model.

Method: After the pig was dead, the abdominal organs block was retrieved. Organs were separated and the block, composed by kidneys, aorta and inferior vena cava was prepared at the back-table and perfused with heparinized (10,000UI) perfusion solution (Celsior 1L). The back-table surgery consisted in the ligation of collateral branches from aorta and inferior vena cava, ligation of perirenal fat, proximal aortic stump ligation and distal aortic stump cannulation (Fig 1a). The perfusion was performed with PerKidney machine perfusion (PerLife, Aferetica s.r.l, Bologna, Italy). During the hypothermic oxygenated perfusion was set a target pressure (P) of 50 mmHg and a target flow (F) of 100ml/min. Normothermic perfusion, as a simulation of transplant, was performed setting a target P of 75 mmHg and a target F of 500ml/min.

Results: The no-flow period lasted 35min, back-table surgery lasted 27.5 ±3.5 min. The hypothermic perfusion lasted 110 min: the mean temperature (T) during perfusion was 6.8 ±1.4 °C, the mean F was 120.4 ±58.7 ml/min, the mean P was 40.3 ±11.2 mmHg and the mean resistance (R) was 0.37 ±0.26 mmHg/ml/min. R started at 1.07, dropped down after 55min concluded at 0.06. Parameters during hypothermic perfusion are reported in figure 2a. The normothermic perfusion lasted 49 min: the mean T was 35.3 ±1.5 °C, the mean F was 495 ±11 ml/min, the mean P was 18 ±8 mmHg and the mean R was 0.031 ±0.016 mmHg/ml/min. R started at 0.05, dropped down after 10min and concluded at 0.01. During the perfusion kidneys gradually changed in color (Fig 1b-1c). Parameters during normothermic perfusion are reported in figure 2.

Conclusion: In this preliminary proof of concept on a large animal model the dual kidney en-bloc perfusion appears feasible. The decreasing of R, the maintenance of F and P, changing in color are favorable characteristics supporting this option, potentially useful in case of lack of devices and contemporary donations. Larger experience is needed for a better setting of parameters during the perfusion and surgical technique.
313.13
Quantification of Center Agressiveness in Accepting Suboptimal Kidney Donations From Deceased Donors in the US

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Purpose: Understanding center-level differences in usage of marginal deceased donor kidneys can help centers increase their deceased-donor transplant rate (DDKT), and to direct SOK offers to centers willing to accept them.

Methods: We studied 5,646,748 offers of 8,539 SOK donors from 1/1/2018-12/31/2019 using SRTR data. Pediatric centers, center annual volume<1, or multiple match-runs were excluded. We defined SOK offer as: age>60, cold ischemia time (CIT)>24 hours, hepatitis C (HCV), serum creatinine (Scr)>2.0 mg/dL, donated after cardiac death (DCD), KDPI>85, or infectious risk donors (IRD). We used multilevel logistic regression to calculate the median odds ratio (MOR), a measure of center-level variation, for each subtype of SOK.

Results: There were 18,471 (64%) SOK among 28,676 DDKT performed, Among 197 centers, the percentage of SOK acceptance ranged from 0 to 44.7% with the median (IQR) of 10.6% (6.9%, 14.6%). The SOK subtype with the least center-level variance was DCD (acceptance range: 0-95%, median [IQR]: 10.2% [6.4%, 15.9%], MOR=2.11) and IRD (acceptance range: 0-63.6%, median [IQR]: 16.0% [9.2%, 22.5%], MOR=2.11). The SOK subtype with the most center-level variance was CIT>24 (acceptance range: 0-55.1%, median [IQR]: 2.7% [0.6%, 6.6%], MOR=3.15). For comparison, the MOR of non-SOK kidneys was 1.90.

Conclusions: There was substantial center-level variation in acceptances of SOK offers for each of the SOK subtype categories. Informing centers of donor phenotypes for which that center’s acceptance rate is lower than the national average may motivate centers to accept more marginal kidneys, improving access to DDKT for patients at those centers.

313.14
Trends in Kidney Transplant Usage After KAS Implementation: Is There Evidence for a KDPI Shift Over Time?

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Background: The Kidney Allocation System (KAS) was implemented in 2014, modifying allocation and introducing the Kidney Donor Profile Index (KDPI) as a metric of organ longevity and graft failure. KDPI >85% predicts a higher risk of graft failure, which may result in a negative labelling effect. High discard rates over time could engender a drift in the metric wherein “riskier” kidneys are not included in the pool and lower risk donors would then be associated with a higher score. We sought to determine transplant rates according to KDPI, changes in sharing according to KDPI, and characteristics of organs used in the pre and post KAS eras.


Results: Despite an initial decline in the average KDPI utilized after implementation of KAS for allocation in Era 3, a rebound occurred, resulting in an overall higher average KDPI used for transplant in Era 5 than pre-KAS (p<0.01). KDPI >85% usage similarly declined from Era 1-4, with recovery in Era 5 (p<0.01). Donor age >60, diabetes, and hypertension showed similar declines early post-KAS with recovery in the final era. The proportion of DCD donors, HCV Ab and NAT positivity, and elevated donor terminal creatinine increased in each subsequent era. Overall, there were no significant differences in median KDRI according to KDPI group from 2010 to 2020 to suggest a “KDPI drift” (See Figure 1). Since KAS, sharing increased across all KDPI groups, but was more pronounced with increasing KDPI.

Conclusion: After initial dips in utilization of high KDPI organs after KAS implementation, trends reversed with higher mean KDPI and proportion of KDPI>85% utilization in the most recent era. Growth in utilization of DCD and HCV (Ab+ and NAT+) organs has occurred over time. Overall, we did not find evidence for a shift to increasingly risk-averse practices according to KDPI following KAS, and changes in regional utilization suggest better direction of these organs to programs willing to utilize them. Further changes are still need to achieve the goal of significantly reducing discard rates for high KDPI organs.
Cost-Effectiveness of Interventions to Increase Utilization of Kidneys From Deceased Donors With Primary Brain Malignancy in an Australian Setting

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Introduction: Kidneys from potential deceased donors with brain cancer are often foregone due to concerns of transmission risk to recipients. This may be due to uncertainty around donors’ medical history and their absolute transmission risk, or risk-averse decision-making among clinicians. However, transmissions are rare and prolonging waiting time for recipients is harmful.

Method: We assessed the cost-effectiveness of increasing utilization of these potential donors using a Markov model patient simulation (Figure 1) to estimate costs and consequences from a payer perspective (Australian government) using linked transplant registry data. We estimated costs and quality-adjusted life-years (QALYs) from three interventions: decision support for clinicians in assessing donor risk, improved data accuracy with real-time data-linkage to hospital records and cancer registries, and increased risk-tolerance to allow intermediate-risk donors.

Results: Decision support increased donation 0.3% with a 2% transmission rate and was dominant (improved QALYs and cost-saving) in 56% of simulations (Figure 2). Real-time data-linkage increased donation 0.6% with 1.8% transmissions and was dominant in 57% of simulations. Increasing risk tolerance increased donation by 2.1% with 3.3% transmissions and was dominant in 75% of simulations (mean +10.0 QALYs and $1.2m ($904k USD) cost-savings).

Conclusion: Accepting intermediate-risk donors with brain cancer is likely to improve patient outcomes and reduce overall healthcare expenditure.

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Glycocalyx Damage Marker Syndecan-1 Correlates With Early Allograft Dysfunction During Hypothermic Liver Machine Perfusion

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Introduction: The endothelial glycocalyx is mainly consisting of Syndecan-1 (Sdc-1) which is released into human serum upon glycocalyx degradation. Glycocalyx alterations are connected to different aspects of organ damage and have been recently investigated in the context of liver transplantation. Due to shortage of donor organs, new preservation methods as hypothermic oxygenated machine perfusion (HOPE) have been introduced to enable transplantation of organs with a higher risk profile. For safe expansion of the donor pool, reliable organ assessment markers for evaluation during machine perfusion are missing. We aimed to measure glycocalyx damage during hypothermic liver perfusion.

Methods: HOPE was performed with the Organ Assist® perfusion system on 40 livers, prior to organ transplantation. Samples were collected during (perfusate at 0 and 60 min) and after HOPE (effluent). Sdc-1 concentration in samples was measured by ELISA as indicator for glycocalyx destruction. We compared clinical parameters with Sdc-1 levels in patients regarding the development of early allograft dysfunction (EAD) using Mann-Whitney U test, Pearson correlation and receiver operating characteristics (ROC).

Results: The 13 patients which developed EAD, showed an elevation in Sdc-1 concentration compared to those without EAD could be shown. No association of graft survival with Sdc-1 (p=0.339) was detected in cox regressions was indicated by ROCs: during HOPE at 60 minutes: (AUC=0.704) vs. 443 (±226) ng/ml; p=0.016, as well as afterwards in the effluent: [2074 (±598) vs. 276 (±150) ng/ml; p=0.076] and 60 min: [1099 (±739) vs. 1773 (±1273) ng/ml; p=0.001 (n=15, 4 with EAD)]. Concentration of Sdc-1 during HOPE correlated with EAD at 0 min: (R=0.433, p=0.006), at 60 min: (R=0.471, p=0.003) and in the effluent: (R=0.769, p<0.001, n=15, 4 with EAD). Furthermore, an association between EAD and Sdc-1 concentrations was indicated by ROCs: during HOPE at 60 minutes: (AUC=0.704 and p=0.018) and in the effluent: (AUC=1 and p=0.004 (n=15, 4 with EAD)). No association of graft survival with Sdc-1 (p=0.339) was detected in cox regression analysis however, reduced graft survival (log-rank=0.009) of EAD patients compared to those without EAD could be shown.

Conclusion: We found that measuring glycocalyx degradation during HOPE could indicate transplantation outcome regarding EAD. Consequently, we argue that Sdc-1 could be a useful biomarker for organ assessment during HOPE.

Outcome of 250 Lung Transplants in Saudi Arabia, 92% Marginal Donors

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Purpose: A total of 250 lung transplantations (LTx) were performed at a single center in Saudi Arabia. 92% of our donors are marginal. The criteria of deceased brain dead donors represent unique differences that bring unique challenges. This report highlights the challenges, management strategies and outcomes.

Methods: The LTx Program at King Faisal specialist hospital was established in 2000 as the first and only active program in Arabian countries. Over the last 12 years the program has witnessed rapid growth. Retrospective review of 250 patients and their donors that underwent LTx at our center between January 2000 and February 2022.

Results: The most common indication for LTx was pulmonary fibrosis (40%), followed by cystic fibrosis (CF)-related bronchiectasis (24%), non-CF-related bronchiectasis (21%), chronic obstructive pulmonary disease (4%), sarcoidosis (3%), Microthiasis (3%). The indicators in other patients included pulmonary capillary hemangiomatosis, lymphangioleiomyomatosis, and retransplantation. Only 39% of our lung transplant recipients had a normal BMI of 18–28 kg/m2, whereas 61% were either overweight with a BMI of <18 kg/m2 (42%) or overweight with a BMI of >28 kg/m2 (19%). Regarding Lung donors (LDs) 92% of our lungs were marginal. 10% age>55 years, 16% PO2 < 300 mmHg, 32% abnormal CXR, 22% Purulent secretions on bronchoscopy, 83% Prolonged ventilation > 5 days with a mean duration of mechanical ventilation (MV) of 9±7 (days). Bacterial colonization was noted in 74% of LDs, including multidrug-resistant bacteria such as acinetobacter (31%), kibisellae (24%) and pseudomonas (12%). Size mismatch was a challenge, 72% required lung volume reduction. In 9 cases bilateral lower lobar Tx, a unilateral lobarTx with contralateral whole lung in 15 cases, the rest required lung trimming. Over the last 7 years extra-corpooreal membrane oxygenation (ECMO), was used in 24% of our LTx as a rescue strategy for grade 3 primary graft dysfunction with 30 days survival of 92% and 1 year survival 88%. Ex vivo lung perfusion was used to expand our pool of LDs, 11 successful cases from 23 attempts were performed over the last 5 years. In spite of the liberal utilization of marginal donors and prolonged post lung transplantation mechanical ventilation (Median (range))11 (1–145 days), length of ICU stay 14 (3–145) and length of hospital stay 36 (12–168), our 30 days, 90 days, 1 year, 3 years and 5 year survival rates were 94.5%, 89%, 87.5%, 76% and 62.5% respectively.

Conclusion: Shortage of good donors forced us to use extended criteria to transplant high risk patients. The selective use of Ex vivo and ECMO helped to achieve comparable results. Prolonged ventilated donors even with bacterial colonization can be utilized for LTx, size mismatch can be overcome by different surgical techniques.

Number of lung transplants reported by year-KFSHRC
Response to a Pandemic: The Fall and Rise of Kidney Transplantation in the United States

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Background: Following the outbreak of COVID-19 in the United States, the number of kidney waitlist additions and living-donor and deceased-donor kidney transplants (LDKT/DDKT) decreased substantially but began recovering within a few months. Since then, there have been several additional waves of infection, most notably, the Delta and current Omicron surge beginning in August and December 2021, respectively. By 1/12/2022, the Omicron surge peaked at 802,699 confirmed new cases, compared to a pre-Omicron peak of 251,772 confirmed new cases on 1/8/2021, demonstrating an immense disease burden on the American population that could have been enough to disrupt transplant practices.

Methods: Using data from the Scientific Registry of Transplant Recipients (SRTR), we compared observed waitlist registrations, waitlist mortality, waitlist removal, LDKT, and DDKT in the United States over four distinct pandemic waves to expected events based on calculations from pre-pandemic and non-wave pandemic data, while accounting for seasonality and secular trends. Four distinct time periods/waves of high COVID-19 incidence in the United States were identified for analysis. Wave 1 was defined March 15, 2020 – May 31, 2020; Wave 2 was defined December 1, 2020 – January 31, 2021; Wave 3 was defined August 1, 2021 – September 30, 2021; and Wave 4 was defined December 1, 2021 – January 31, 2022. Waves 1, 2, 3, and 4 were referred to as the Initial, Winter 2021, Delta, and Omicron waves during our analysis.

Results: Although the number of daily waitlist additions has been increasing since May 2020, the size of the active waitlist has consistently declined, reaching a minimum of 53,180 on 1/31/2022. The recent Omicron surge knocked LDKT from 12% below expected (IRR = 0.820.880.95) during the Delta wave to 34% below expected (IRR = 0.610.660.71). DDKT, in contrast, was relatively unaffected by the Omicron wave (IRR = 0.830.870.91 and 0.820.850.89 during the Delta and Omicron waves, respectively). Waitlist death declined from 20% above expected (IRR = 1.111.201.30) during Delta to 19% below expected (IRR = 0.740.810.89) during Omicron, whereas waitlist removal remained at expected levels throughout both (IRR = 0.951.041.13 and 0.991.081.18 during Delta and Omicron, respectively). Note, this was the first time that an outcome returned to expected levels since the start of the pandemic.

Conclusions: The Omicron wave brought substantial declines in DDKT and LDKT that have not been seen since the Initial wave. Due to vaccine mandates in place at many transplant centers across the nation, the American SRTR population now has high levels of vaccination including high levels of second and third booster shots. Hence, despite the Omicron wave’s exceptionally high COVID-19 infection incidence in the American national cohort, there was no increase in waitlist mortality, likely due to vaccination.

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Table 1. Observed events as a proportion of expected events, March 15, 2020 - January 31, 2022. Bold denotes statistically significant IRRs.

<table>
<thead>
<tr>
<th>COVID-19 Wave</th>
<th>Waitlist Registration</th>
<th>DDKT</th>
<th>LDKT</th>
<th>Waitlist Removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wave 1</td>
<td>0.074.25</td>
<td>0.68.30</td>
<td>0.68.30</td>
<td>0.36.41</td>
</tr>
<tr>
<td>Wave 2</td>
<td>0.98.91</td>
<td>0.98.91</td>
<td>0.75.82</td>
<td>0.6.63.72</td>
</tr>
<tr>
<td>Wave 3</td>
<td>0.99.91</td>
<td>0.87.81</td>
<td>0.86.90</td>
<td>0.81.20.82</td>
</tr>
<tr>
<td>Wave 4</td>
<td>0.97.91</td>
<td>0.80.89</td>
<td>0.66.71</td>
<td>0.81.89</td>
</tr>
</tbody>
</table>
MTOR Inhibitors Promote Highly Functional T Cell Immunity in Kidney Transplant Recipients Vaccinated Against COVID-19

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Introduction: Kidney transplant recipients (KTRs) are highly vulnerable to severe COVID-19, however are poorly protected by vaccination. Additional vaccine doses have achieved limited improvements in serological neutralisation or T cell response. A novel strategy to boost vaccine response is needed. Inhibition of mechanistic target of rapamycin (mTOR) has been found to enhance the formation of memory T cells following vaccination of non-human primates.

Methods: KTRs and age-matched healthy controls (HC) were recruited from a transplant centre in South Australia to undergo a 2-dose vaccination schedule with BNT162b2 or ChAdOx1. KTRs were receiving standard-of-care (SOC) triple therapy (tacrolimus, mycophenolate mofetil, prednisolone; n=15), sirolimus-inclusive (n=15), or everolimus-inclusive (n=11) protocols. Patients on mTORi-inclusive protocols were most commonly receiving sirolimus or everolimus, mycophenolate mofetil, and prednisolone. Following 2 vaccine doses, spike-specific IgG and T cell responses (by IFNγ ELISpot) were measured to assess vaccine immunogenicity, and live virus neutralisation and anti-receptor binding domain (RBD) IgG (Elescys, Roche) were evaluated as correlates of protection from infection and disease. Function and phenotype of antigen-specific T cells were further interrogated by flow cytometry.

Results: KTRs on mTORi-inclusive protocols demonstrated improved humoral immunity, with 46.7% and 63.6% seroconversion rates in the sirolimus and everolimus groups, respectively, compared with 26.3% in the SOC group. This was mirrored by improved serological neutralisation of live SARS-CoV-2 virus (ancestral strain) by patients on mTOR inhibitors. Serological neutralisation of the Omicron variant was achieved by 20% of KTRs on sirolimus, but by none in the SOC nor everolimus groups. Remarkably, sirolimus use was associated with a median antiviral T cell response 55-fold greater than SOC therapy, and 5-fold greater than HC. SARS-CoV-2-specific CD4+ and CD8+ T cells in these patients were highly polyfunctional and formed robust central memory out to 3 months post second vaccine dose. While the phenomenon of antigen-specific memory T cells from KTRs on SOC therapy was skewed relative to healthy individuals, this abnormality was corrected in the sirolimus group.

Conclusions: These data support a randomised controlled trial of immunosuppression modification with sirolimus as a strategy to directly improve vaccine responses in KTRs.

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314.4

How Did the Omicron Wave Impact Kidney Transplant Recipients? A Comparative Analysis From a Prospective Cohort Single-Center Study

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Introduction: The first two years of the SARS-CoV-2 pandemic were marked by an unprecedented impact on the survival of the kidney transplant patient worldwide, a population that accumulates risk factors for worse outcomes and has reduced vaccine response. However, from the end of 2021, the pandemic acquired new nuances, with the broad availability of booster doses of the vaccine – in Brazil, since 08/26/2021 – and the emergence of the Omicron variant, more infectious but possibly less lethal. The aim of our study was to describe how the new era of the pandemic differed from the previous one in a large cohort of renal transplant patients being followed up at a single center.

Methods: This single-center prospective cohort study included kidney transplant recipients with confirmed COVID-19 between 03/20/2020 and 02/15/2022. The outcomes of interest were incidence of confirmed SARS-CoV-2 infection, need for hospitalization, mechanical ventilation, dialysis and COVID-19 associated death within 28 days from the onset of symptoms. For the present analysis, we arbitrarily separated the patients into two eras, named “Era 1” (03/20/2020 to 12/02/2021) and “Era 2” (12/17/2021 to 02/15/2022), considering the emergence of the Omicron variant in Brazil at the end of the year 2021 and that there were no cases registered between 12/02/2021 and 12/17/2021. Genetic sequencing to identify the variants was not available in the center.

Results: Among the 10,497 kidney transplant recipients in follow up, there were 3,327 cases of confirmed COVID-19 in the entire observation period. There was an increase in the incidence rate from 0.3 cases/1000patients-day in Era 1 to 1.72 cases/1000patients-day in Era 2, and the sharp increase in the number of cases in the last Era is demonstrated in Figure 1. There was no difference in the median age (51 [IQR 42-60] years versus 50 [IQR 40-61] years, p=0.447) or in the proportion of male patients (60.4% versus 58.5%, p=0.294) between the two Eras. There was a significant decrease in the rate of hospitalization (57.5% versus 29.2%, p<0.0001), need for mechanical ventilation (29.9% versus 16.3%, p<0.0001), dialysis (25.6% versus 9.1%, p<0.0001) and COVID-19 related death (26.9% versus 10%, p<0.0001, as demonstrated in Figure 1).

Conclusion: There was a clear change in the dynamics of the pandemic from December 2021 among renal transplant patients, with higher incidence and lower severity of COVID-19, possibly due, but not limited to, booster vaccination and lower pathogenicity of the Omicron variant.

314.5

The Difference Between Delta and Omicron Variants in Solid Organ Transplant Recipients

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Introduction: Solid Organ Transplant (SOT) recipients are vulnerable to SARS-CoV-2 infection. Delta variant has been reported to have worse outcomes as compared to other variants to date. The Omicron variant has been reported more transmissible but less virulent in general population. However, this phenomenon has not been validated in SOT recipients.

Method: This is a retrospective cohort study, conducted in two phases, between July 1st and December 10th, 2021(Delta dominant phase), and January 1st and January 31st, 2022(Omicron dominant phase) in one of the biggest SOT centers in the United States. Patient demographics including transplanted organ, immunosuppressive medication, vaccination status, and treatment modalities were obtained. We also compared clinical outcomes including hospitalization, ICU admission rate and mortality between two groups. Chi squared or fisher’s exact test were performed for categorical variables, whichever appropriate. For continuous variables, Mann Whitney U-test was performed. Multiple logistic regression model with stepwise backward elimination was developed to identify the risk factors for mortality. We put put variables whose p value was less than 0.2. Of note, the institutional treatment protocol has not changed during the study period.

Result: We identified 64 and 95 SOT recipients while delta and omicron variants were dominant, respectively. The rate of kidney transplant, age, gender, African American race, and the rate of at least received one dose vaccination were not significantly different between two groups. Of note, the hospital admission rate (68.8% vs 36.2%, p<0.001), ICU admission rate (20.3% vs. 6.3%, p=0.012), and mortality (20.9% vs. 4.2%) were higher during the delta variant versus omicron variant phase. For the risk factor analysis for mortality, we put age, African American race, COVID-19 variant, kidney transplant and vaccination status into multiple logistic regression model. Finally, delta variant was the only statistical significant risk factor for mortality (p<0.001, Odds ratio 9.35, 95% confidence interval 2.52-34.5).

Conclusion: This is the first study comparing the outcomes between Delta variant dominant and Omicron variant dominant phase in SOT recipients. Even though there was no treatment protocol changed, the identified risk factor for mortality was delta variant dominant phase. However, still, the hospital admission rate (36.2%) should have been observed while Omicron variant phase and required significant aggressive treatment. Thus, we should prepare and may need to change the treatment protocol on base of the variant in the future.
Factors Effecting Mortality Among COVID-19 Patients in Renal Transplant Recipients From a Single Center in Pakistan

Sunil Dodani1, Asma Nasim1, Tahir Aziz2.
1Infectious Diseases, Sindh Institute of Urology and Transplantation, Karachi, Pakistan; 2Transplant Nephrology, Sindh Institute of Urology and Transplantation, Karachi, Pakistan.

Introduction: Corona virus disease-19 (Covid-19) has significantly affected organ transplantation with concerns regarding severe infection and mortality. Data on Covid-19 in renal transplant recipients (RTRs) is scarce from Pakistan. The aim of this study is find out the factors effecting mortality among Covid-19 patients in renal transplant recipients from the largest transplant center of Pakistan.

Methods: All RTRs >18 years, with positive severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) polymerase chain reaction (PCR) and diagnosed as severe disease, between April to December 2020 were retrospectively reviewed. The severe disease was defined as O2 saturation <94% at room air on admission. Survivors and non-survivors were compared. Demographics, immunosuppression, comorbid conditions, clinical features, laboratory investigations, and graft function were noted.

Results: A total of 95 RTRs had severe disease. There was no difference in mortality between age, gender, and co-morbid conditions among survivors and non-survivors. Both groups received a similar immunosuppressive regimen. Intensive care unit (ICU) admission [16.5% vs 68.8% p<0.001 OR 11.17 95% CI (3.3-37.6)] and high D-dimers >1.5µg/ml (p=0.05) at the time of admission were significantly associated with mortality. There was no association of graft function with mortality. Treatment with methyl-prednisolone was found to be significantly associated with survival [83% vs 43% P=0.02 OR 0.15 95% CI (0.05-0.49), Table 1] WHO grading of the disease is shown in figure 1, there was a 100% mortality among patients on a mechanical ventilator.

Conclusion: ICU admission and high D-dimers at the time of admission are the significant risk factors for mortality in patients with Covid-19 infection. There was no association of graft dysfunction with mortality. Steroids use has significantly improved survival in renal transplant recipients with severe Covid-19 infection.

| Table 1: Comparison between survivors and non-survivors among patients with severe disease n=95 |
|---------------------------------|---------------------------------|---------------|-----------------|---------------|
| Characteristics                | Survivor                        | Non-survivor  | p-value | OR (95% C.I.) |
| Age mean ±SD                   | n=79 (%)                        | n=16 (%)      |         |               |
| < 30                           | 39.5 ± 11.5                     | 37.9 ± 9.5    | 0.60   | -             |
| > 50                           | 19 (24.1)                      | 4 (25.0)     | 0.58   | 1.1 (0.3-3.6) |
| Male                           | 46 (58.2)                      | 13 (80.8)    | 0.43   | 1.0 (0.5-4.9) |
| Diabetes mellitus              | 5 (6.3)                        | 2 (12.5)     | 0.335  | 2.1 (0.37-12.0) |
| Hypertension                   | 58 (73.4)                      | 12 (75.0)    | 0.999  | 1.1 (0.3-3.7) |
| Induction                      | 13 (16.5)                      | 3 (18.7)     | 0.5    | 1.2 (0.2-4.7) |
| Maintenance immunosuppression  |                                |               |        |               |
| Cytosporines based             | 30 (38.0)                      | 6 (37.5)     | 0.97   | 0.8 (0.3-2.0) |
| Tacrolimus based               | 13 (16.5)                      | 4 (25.0)     | 0.476  | 1.7 (0.47-6.1) |
| Azathioprine based             | 51 (64.6)                      | 10 (62.5)    | 0.876  | 0.9 (0.3-2.8) |
| MMF based                      | 16 (20.3)                      | 2 (12.5)     | 0.728  | 0.6 (0.12-2.73) |
| mTOR inhibitor based           | 10 (12.7)                      | 3 (18.8)     | 0.454  | 1.6 (0.39-6.59) |
| ICU admission                  | 13 (16.5)                      | 11 (68.8)    | <0.001 | 11.17 (3.3-37.6) |
| Treatment                      |                                |               |        |               |
| Methyl prednisolone            | 66 (83.5)                      | 7 (43.8)     | 0.002  | 0.15 (0.05-0.49) |
| Toctilizumab                   | 40 (50.6)                      | 9 (56.3)     | 0.682  | 1.25 (0.42-3.97) |
| IV 1g G616                     | 39 (49.4)                      | 9 (56.3)     | 0.32   | 0.32 (0.15-0.67) |
| Remdesivir                     | 12 (15.2)                      | 4 (25.0)     | 0.462  | 1.861 (0.514-6.75) |

Laboratory parameters on Admission

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Non-survivors</th>
<th>p-value</th>
<th>OR (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALC &lt;1000</td>
<td>19 (50)</td>
<td>5 (71.4)</td>
<td>0.422</td>
<td>0.400 (0.069-2.322)</td>
</tr>
<tr>
<td>BUN &gt; 30</td>
<td>18 (47.6)</td>
<td>4 (44.4)</td>
<td>0.999</td>
<td>1.125 (0.261-4.848)</td>
</tr>
<tr>
<td>CRP &gt; 7</td>
<td>16 (64.0)</td>
<td>6 (75.0)</td>
<td>0.687</td>
<td>0.593 (0.098-3.573)</td>
</tr>
<tr>
<td>Ferritin &gt; 1000</td>
<td>8 (34.8)</td>
<td>4 (44.4)</td>
<td>0.696</td>
<td>0.667 (0.193-2.204)</td>
</tr>
<tr>
<td>D-dimer &gt; 150</td>
<td>3 (20)</td>
<td>5 (71.4)</td>
<td>0.052</td>
<td>0.100 (0.003-0.370)</td>
</tr>
<tr>
<td>Serum creatinine (Median IQR)</td>
<td>2.21 (1.45-4.05)</td>
<td>4.3 (3.0-5.4)</td>
<td>0.104</td>
<td>-</td>
</tr>
<tr>
<td>AKI</td>
<td>40 (51.3)</td>
<td>10 (62.5)</td>
<td>0.413</td>
<td>0.632 (0.209-1.907)</td>
</tr>
</tbody>
</table>
Outcomes of SARS-CoV-2 in Hospitalized Solid Organ Transplant Recipients During the Omicron Wave in the United States

Walea Dabbas1, Preerna Kumar1, Ruchi Naik2, Dana Pierce2, Kristin Haagler3, Benito Valdenegros2, Scott Benken3, Ignatius Tang1.
1Nephrology, University of Illinois at Chicago, Chicago, IL, United States; 2Pharmacy, University of Illinois at Chicago, Chicago, IL, United States.

Introduction: Though SARS-CoV-2 mRNA vaccine has been effective in reducing the severity of COVID-19 and associated hospitalization and mortality in the general population. Its effectiveness in the solid organ transplant recipients is not well studied. Here, we are presenting our outcome data of SARS-CoV-2 patients hospitalized during the omicron wave in a tertiary care center in the United States.

Method: We conducted a single center retrospective analysis of the effectiveness of SARS-CoV-2 mRNA vaccine in the hospitalized patients of kidney and simultaneous Kidney and Pancreas (SPK) Transplant recipients from December 1, 2021 to February 25, 2022 during the Omicron wave. Patients were categorized according to the SARS-CoV-2 vaccination status at time of admission: 1. Fully vaccinated—completion of 3 doses of SARS-CoV-2 mRNA vaccine. 2. Partially vaccinated—1 or 2 doses of SARS-CoV-2 mRNA vaccine. 3. Unvaccinated. The data including demographics, clinical presentation and the course along with mortality were collected using electronic medical records. Standard statistical analysis was done.

Results: There were 49 kidney and SPK recipients hospitalized with SARS-CoV-2. The majority of patients were African American and Hispanic with the mean age of 51.9 +/- 12.6 years, out of which 21(42.8%) were females. Fourteen (8.1%) patients were within one year post transplantation period. Twenty-eight (57%) patients required oxygen therapy, 13 (26.5%) patients were admitted to the intensive care unit (ICU), out of which 10 (20.4%) patients died. Twenty-two (44.9%) patients were fully vaccinated, 19 (38.7%) were partially vaccinated, and 8 (16.3%) were unvaccinated (TABLE). In the fully vaccinated group, 11 (50%) patients required oxygen therapy, 3 (14%) patients admitted to the ICU and 2 (9%) died. In the partially vaccinated group, 12 (63%) patients required oxygen, 8 (42%) admitted to the intensive care unit and 6 (32%) died. In the unvaccinated group 5 (63%) required oxygen therapy, 2 (25%) patients were admitted to the intensive care unit and subsequently died. One fully vaccinated patient and 2 partially vaccinated patients were admitted to the ICU for hyperglycemia management rather than COVID-19 related symptoms.

Conclusion: The Kidney and SPK transplant recipients who completed the primary series of SARS-CoV-2 mRNA vaccine (3 doses) had better outcomes. We may conclude that for immunocompromised patients vaccination can reduces the severity of COVID19 and associated mortality.

<table>
<thead>
<tr>
<th>n=49</th>
<th>Not vaccinated (8)</th>
<th>Partially vaccinated (15)</th>
<th>Fully vaccinated (22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age in yr (median)</td>
<td>48.5 (47)</td>
<td>50.6 (51)</td>
<td>53.5 (54)</td>
</tr>
<tr>
<td>Male</td>
<td>7</td>
<td>88%</td>
<td>9</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>13%</td>
<td>10</td>
</tr>
<tr>
<td>Asian</td>
<td>0</td>
<td>0%</td>
<td>0</td>
</tr>
<tr>
<td>African American</td>
<td>6</td>
<td>75%</td>
<td>11</td>
</tr>
<tr>
<td>Caucasian</td>
<td>0</td>
<td>0%</td>
<td>0</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2</td>
<td>25%</td>
<td>8</td>
</tr>
<tr>
<td>Oxygen requirement</td>
<td>5</td>
<td>63%</td>
<td>12</td>
</tr>
<tr>
<td>ICU admission</td>
<td>2</td>
<td>25%</td>
<td>8</td>
</tr>
<tr>
<td>Mortality</td>
<td>2</td>
<td>25%</td>
<td>6</td>
</tr>
</tbody>
</table>

The Adverse Effects of High Dose Corticosteroid on Infectious and Non-infectious Sequelae in Renal Transplant Recipients With Coronavirus Disease 19 in India

Narayan Prasad1, Vamsi Char Veeranki1, Jayakumar Meyyappan1, Dharmendra Bhadauria1, Manas R Behera1, Ravi Kushwaha1, Manas R Patel1, Monika Yaccha1, Anupama Kaul1.
1Nephrology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, LUCKNOW, India.

Introduction: The corticosteroid dosing modulation in renal transplant recipients (RTR) with COVID-19, was not well defined. We aimed to analyze the outcomes, infectious and non-infectious sequelae in RTR with COVID-19 with reference to corticosteroid dosing and the first and second pandemic wave of COVID-19.

Material and methods: This study included the RTR admitted during the two pandemic waves between March 25, 2020, and July 31, 2021. Patients were categorized into mild, moderate, and severe COVID 19. The outcomes and predictors of survival at four weeks were analyzed. The survivors were also followed for 6 months and were studied for mortality, readmission rates, infectious and non-infectious sequelae with reference to high-dose and standard-dose corticosteroids.

Results: A total of 251 RTRs, 104 during the first wave and 147 during the second wave, were treated. Overall mortality was 15.1% (11.5% in first wave vs 17.5% in second wave, P= 0.23). The use of high-dose steroids was also significantly high in non-survivors (85.8% vs 11.3%, P=0.001). On multivariate analysis, the severity of COVID-19, graft dysfunction, and high dose of corticosteroid therapy were associated with increased odds for mortality. Amongst survivors, 6-months mortality (17.3% vs 0.5%, P= 0.001), readmission rate (91.3% vs 23.7%, P=0.001), fungal infection (30.4% vs. 2.2% p < 0.001), post-COVID lung sequelae (21.7% vs. 4.4%, P = 0.008) were significantly higher in the high-dose corticosteroid group than the standard-dose group.

Conclusion: The high-dose corticosteroid dosing in the RTRs with COVID-19 was associated with increased infectious, particularly fungal infections, non-infectious sequelae with higher mortality on subsequent follow-up.

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1Chief Of Nephrology and Renal transplant, Hospital General de Aguados Cosme Argerich, Caba, Argentina; 2Central Laboratory, Hospital General de Aguados Cosme Argerich, Caba, Argentina; 3Unidad de Infectología, Hospital General de Aguados Cosme Argerich, Caba, Argentina; 4División Alimentación, Hospital General de Aguados Cosme Argerich, Caba, Argentina; 5Devision of Nephrology and Renal Transplant, Hospital General de Aguados Cosme Argerich, Caba, Argentina.

Introduction: COVID-19 is diagnosed with a polymerase chain reaction (RT-PCR) test analyzing respiratory samples, with a positive or negative result. Cycle threshold (Ct) values of an RT-PCR assay refer to the number of cycles needed to amplify viral RNA to reach a detectable level. The clinical implications of Ct values are not yet fully understood either for the general population or solid organ transplant recipients.

Objective: To describe the correlation of Ct values with the outcome of a group of transplant (TX) and immunocompetent (IC) patients (Ps).

Methods: Prospective study of TX and IC Ps diagnosed with COVID-19 as confirmed by PCR testing between the 1st and 7th day (mean 2.85) after the onset of symptoms. The Ct of the specific gene for SARS-CoV-2 from the PCR tests was considered. A poor outcome was defined for patients with hypoxemia, mechanical ventilation or progressing to death. A logistic regression analysis, where the dependent variable was the patient’s outcome, was performed. Data were processed with the R Studio v.4.0.5 software (2021).

Results: One hundred and eighty Ps with COVID-19 diagnosis were analyzed: 123 IC and 57 TX; 51% were women and the average age was 49±14, without differences between groups. The mean Ct level of the specific gene was 22.3 ± 6 for TX vs. 25.02 ± 7.1 for IC (p=0.009). The predominant comorbidity in the IC group was diabetes mellitus (DM) in 25%, followed by obesity in 22%, while in the TX group it was high blood pressure (HBP) in 82%, followed by DM in 19%. A significant association between comorbidities and IC was found (Chi² = 9.34; p = 0.002). In a bivariate analysis, the specific gene and the TX and/or IC status were not associated with outcome. Age, sex, presence of comorbidities, C-reactive protein (CRP) and ferritin values were associated with outcome (Table 1). In a multiple analysis, two models were developed: one using CRP and the other ferritin as inflammatory markers. In both models, all the variables were associated with outcome, except for specific gene. The likelihood of a poor outcome increased with older age, higher ferritin and CRP levels, comorbidities, in female Ps and the IC group vs. the TX one (Table 2).

Conclusion: No association between Ct value and outcome was found. The Ct value was lower in the TX group; however, no association was found when analyzing it separately either. Comorbidities and inflammatory markers were associated with a poor outcome. The poorer outcome in the IC group could be accounted for by a higher prevalence of comorbidities and an older average age in this group.
Controlling the Cytokine Storm With Therapeutic Plasma Exchange: The MTI Experience With Solid Organ Transplant Recipients

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Introduction: The solid organ transplant recipient (SOTr) have suffered a tremendous impact from coronavirus pandemic. The use of immunosuppressants and frequent associated medical comorbidities put this population at extreme risk for developing SARS-CoV-2 associated pneumonia. SARS-CoV-2-related mortality is higher in SOT. It has been hypothesized that cytokine release storm (CRS) is the leading cause of ARDS in COVID-19 and timely control of this inflammatory response may improve outcomes. We report our experience of using therapeutic plasma exchange (TPE) to improve outcomes by tackling CRS in a timely manner.

Methods: This is a single-center, retrospective cohort study of SOTr diagnosed with SARS-CoV-2 infection from April 2020 to April 2021. All the patients received severity stratified institutional protocolized treatment and TPE was initiated based on clinical and inflammatory parameters of CRS and ARDS. TPE patients received Methylprednisolone 250 mg x 3 days then 125 mg x 2 days, followed by Prednisone 60 mg x 2 days and then 30 mg x 2 days. All patients received prophylaxis with omeprazole, ivermectin 0.2 mg/Kg daily for 2 days followed by 2 additional doses 2 weeks later, and trimethoprim/sulfamethoxazole (renally adjusted) 3 times weekly for 3 months. Laboratory markers, immunosuppression, WHO severity score pre- and post-TPE therapy and outcomes including mortality were analyzed. For risk factor analysis for mortality, we performed logistic regression analysis for univariate analysis. After that, based on the univariate analysis, we developed multivariate model. We conducted multiple logistic regression analysis with stepwise backward elimination.

Results: 62 patients were followed for median of 141 days (range 8-376). The median age was 60 years (range 28-78), 65% were male, 76% had hypertension, 55% had diabetes and 81% were overweight with a BMI > 25 kg/m2. 90% were of Hispanics and Afro-Caribbean ethnicity. The most common transplanted organ was kidney with 54 patients (87%), followed by liver with 4 patients (6.5%). Time from transplant to diagnosis was 10 months (median, IQR 4-37) and time from symptoms to admission was 3 days (median, IQR 2-5). 79% of the patients were admitted to an intensive care unit (ICU). Tacrolimus (77%) and mycophenolate mofetil (87%) were the most common immunosuppressants used. The median of TPE sessions was 5 (range 1-20). Prior to TPE, there were 27 patients (44%) requiring ventilatory support and additional support (vasopressors, Renal Replacement Therapy (RRT) or Extracorporeal Membrane Oxygenation (ECMO)). A reduction of 32% support on the 27 patients was observed after TPE. The WHO severity score pre- and post-TPE therapy was statistically significant (p<0.001). The overall mortality was 26/62 patients (42%). Secondary infections were diagnosed in 35/62 (56%) of patients with 77% leading to mortality and of those, 38% were fungal infections. The median length of stay was 42 days (range 2-207). 4/54 (7%) kidney transplant recipients developed graft failure at 9, 18, 139 and 344 days respectively; and 4/54 (7%) had episodes of acute rejections at 1,14, 22 and 124 days of COVID diagnosis, respectively. Univariable analysis showed that older age and elevated LDH pre TPE and the lack of decline on LDH, D Dimer, CRP and ferritin values post TPE were risk factors for mortality (p=0.001; 0.022; 0.004; 0.0002 and 0.043, respectively). The presence of a secondary infection was correlated with increased likelihood of death from 25% to 55% and it occurred with a mean of 8 days (range 1-65) from its diagnosis. Multivariate analysis showed older age and CRP values post TPE as risk factors for mortality (p=0.015 and 0.04, respectively).

Conclusion: SARS-CoV-2 infection with cytokine storm leading to ARDS leads to high mortality, especially in the SOT. TPE appears to be a valuable tool to control the cytokine storm by reducing the systemic inflammatory response and improving the overall critical state. Alongside with older age, we observed that high levels of LDH pre TPE and the persistent high levels of the other inflammatory parameters, specifically CRP post TPE and secondary infections, were predictors of mortality. Further research is needed to establish if these findings can lead to clinical guidelines.

<table>
<thead>
<tr>
<th>Table 1. Management and outcomes of SOT recipients with COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHO ordinal clinical severity score</strong></td>
</tr>
<tr>
<td><strong>Pre-TPE</strong></td>
</tr>
<tr>
<td>4: Oxygen by mask or nasal prongs</td>
</tr>
<tr>
<td>5: Not invasive ventilation or high flow mask</td>
</tr>
<tr>
<td>6: Intubation and mechanical ventilation</td>
</tr>
<tr>
<td>7: Ventilation + additional organ support (vasopressors, RRT,</td>
</tr>
<tr>
<td>ECMO)</td>
</tr>
<tr>
<td><strong>Post-TPE</strong></td>
</tr>
<tr>
<td>1: No limitation in activity</td>
</tr>
<tr>
<td>2: Some limitation in activity</td>
</tr>
<tr>
<td>3: Hospitalized. No oxygen therapy</td>
</tr>
<tr>
<td>4: Oxygen by mask or nasal prongs</td>
</tr>
<tr>
<td>5: Not invasive ventilation or high flow mask</td>
</tr>
<tr>
<td>6: Intubation and mechanical ventilation</td>
</tr>
<tr>
<td>7: Ventilation + additional organ support (vasopressors, RRT,</td>
</tr>
<tr>
<td>ECMO)</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
</tr>
<tr>
<td>Ranibizumab</td>
</tr>
<tr>
<td>Tacrolimus</td>
</tr>
<tr>
<td>Dexamethasone IV/PO</td>
</tr>
<tr>
<td>Therapeutic anticoagulation</td>
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<tr>
<td>Convalescent Plasma</td>
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<tr>
<td><strong>TPE treatments, median (range)</strong></td>
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<tr>
<td>5 (0-20)</td>
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<table>
<thead>
<tr>
<th>Table 2: Pre and post TPE values</th>
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</thead>
<tbody>
<tr>
<td><strong>LDL Unit/L</strong></td>
</tr>
<tr>
<td>pre-p022</td>
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<tr>
<td>pre-p022</td>
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COVID-19 in Solid Organ Transplant Recipients: Clinical Presentation, Outcome and Reinfection. Multicenter Study in Argentina

Natalia R Piauato1, Astrid Smud2, Laura Barcán2, Patricia Giorgio2, Melissa Martinez2, Sergio Andino2, Claudia Salgueira1,6,7, Rocio Gago3, Roxana Del Grosso2,8, Martin Azenziosio10, Lucia Cornet1, Elena Temporit11.

1Infectious Diseases, ITAC Diaverum, Caba, Argentina; 2Infectious Diseases, HIBA, Caba, Argentina; 3Infectious Diseases, Central Hospital, Mendoza, Argentina; 4Infectious Diseases, Favaloro Foundation, Caba, Argentina; 5Infectious Diseases, Hospital Británico, Caba, Argentina; 6Infectious Diseases, Sanatorio Anchorena, Caba, Argentina; 7Infectious Diseases, Sanatorio Mitre, Caba, Argentina; 8Infectious Diseases, Hospital Austral, Pilar, Prov Buenos Aires, Argentina; 9Infectious Diseases, Sanatorio Sagrado Corazón, Caba, Argentina; 10Infectious Diseases, Sanatorio Sagrado Corazón, Mendoza, Argentina; 11Infectious Diseases, CEMIC, Caba, Argentina.

Introduction: COVID-19 outcome in solid organ transplant recipients (SOT) is similar to that in the general population. Vaccine effect is not known. We report the experiences in Argentina.

Methods: Retrospective study of national SOT registers. Inclusion criteria: diagnosis of COVID-19 confirmed by RT-PCR. Hypercomorbidity (≥ 5 comorbidities) and immunosuppression (IS) were assessed. NOSA and nosocomial infection were defined. The main end point was in-hospital death. The statistical analysis consisted in the calculation of the frequencies and measures of central tendency and dispersion. The measurement level was applied.

Results: From September 2020 to March 2021, the hospital catered to more than 3000 covid positive patients including previously transplanted patients and 126 new living related renal transplantation surgeries were carried out. Patients were admitted 10 days prior to the surgery in a bioprotective bubble and 3 covid PCR tests were performed 72 hours apart before the surgery. The mean age of newly performed cases was 28.7 ± 8.6 years, with 100 males (79.4%) and 26 females (20.6%). Among all patients, two patients had a history of COVID-19 infection and four more developed it during the post operative period. The hospital stay and renal functions were comparable to the pre-pandemic data from the same unit (Table 1). While the case fatality during the pandemic was 26.7 ± 8.6% vs 34.4% during the pre-pandemic data from the same unit (Table 1). While the case fatality during the pandemic was 26.7 ± 8.6% vs 34.4% during the pre-pandemic data from the same unit (Table 1). While the case fatality during the pandemic was 26.7 ± 8.6% vs 34.4% during the pre-pandemic data from the same unit (Table 1). While the case fatality during the pandemic was 26.7 ± 8.6% vs 34.4% during the pre-pandemic data from the same unit (Table 1). While the case fatality during the pandemic was 26.7 ± 8.6% vs 34.4% during the pre-pandemic data from the same unit (Table 1).

Conclusion: The outcomes of renal transplantation during the covid pandemic are comparable to pre-pandemic statistics.
Nationwide Data on Gender Disparity in Solid Organ Transplantation for India in the Pre-pandemic and Pandemic Era

Sanshriti Chauhan1, Vasanthi Ramesh2, Chaitali Pal3. 
1Nephrology and Transplantation, Institute of kidney disease and research center, institute of transplantation sciences, Ahmedabad, India; 2Founder, Director, NOTTO and HAG Officer, VMMC and Safdarjung hospital, New Delhi, India; 3Former Consultant(R & D), NOTTO, New Delhi, India.

Introduction: Organ donation and transplantation is instrumental but intricately affected by prevailing legal, cultural, socio-economic and health factors. Worldwide trends of gender inequity in organ transplantation exist, with there being more male recipients than female and conversely many more women organ donors than men.

Method: The gender gap in organ donation and transplantation with respect to solid organ transplants specially for kidney, liver, lung, heart, pancreas and small bowel over two time periods of 2019 and 2020 across India was examined through the data submitted annually to the Global database on donation and transplantation (GODT). Living donor transplants highlight this disparity.

Results: Due to the ongoing COVID-19 pandemic situation, the number of transplants, especially living donor organ transplants in India has gone down from 10,608 in 2019 to 6,461 in 2020 and kidney donation comprises about 3/4th of total living organ donations. However, the relative share of women accounting for around 65% of total living organ donors remains. Distinctly, women donors account for around 65% of living kidney donors (5633/8613) and 54% of living liver donors (1084/1993) in 2019, the share of which increased fractionally in 2020 [(3352/4970)67.4 and (832/1489)55.9% respectively]. There were 6,717 women donors out of 10,608 total donors in 2019, the corresponding share of which was 4,184 out of 6,461 in 2020. Amongst the transplant recipients, females account for only 27% in both the years with the share of women recipients from deceased donors being slightly higher (around 29.5% and 28% in 2019 and 2020 respectively). Women account for 28% of recipients of living donor kidney transplants with the share of deceased donor transplants being slightly higher (34 and 32.6% respectively in 2019 and 2020). Women comprise only one fourth of total liver transplant recipients. The number of heart, lung, pancreas and small bowel transplants in India are quite low with varying shares of female recipients.

Conclusion: There exists prominent gender disparity in the sphere of organ donation with women comprising roughly 75% of the total donor pool and conversely only 27.6% of all organ transplant recipients. The gender gap in living transplants is higher than that for deceased organ transplants. There is a need for action to eliminate gender disparity in organ transplantation for the disparity exists not only among patients but among physicians and surgeons as well.

Analysis of ABO-Incompatible Kidney Transplantation in Post-covid-19 Candidates: A Multicentre, Retrospective Cohort Study From India

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Introduction: There is a dearth of data regarding the consequences of ABO-incompatible kidney transplant (ABOiKTx) amongst post-COVID-19 candidates.

Methods: The study was designed as a retrospective, multi-centric cohort study across 11 sites in India, from August 2020 to December 2021. The data for ABOiKTx conducted for post-COVID-19 candidates were investigated. The primary outcome of biopsy-proven acute rejection (BPAR) was compared with the ABO protocol implemented through Kaplan Meier (KM) analysis. The secondary outcomes were graft loss, patient survival, and infections.

Results: A total of 38 ABOiKTx with candidates of median (Interquartile range) age as 38.5(31.25-47.5) years were performed. 19 cases had a mild illness of COVID-19 severity, while nine (23.6%) had oxygen requirement. Six (15.7%) donors also were post-COVID-19. The most common ABO incompatibility reported was A to O in 14(36.8%) pairs followed by B to O in 10(26.3%) pairs. The maximum isoagglutinin titer cut-off was 1:2048 and 1:64 for baseline and pre-transplant levels respectively. The median time from COVID-19 infection to surgery was 130(63.2-183) days. BPAR, graft loss, and mortality were 13.1%, 2.6%, and 2.6% respectively. The Breslow-Wilcoxon’s p-value in KM plots were 0.57 and 0.93 for thymoglobulin-based induction and high dose rituximab-based regimen respectively. The incidence of re-infection was 2.6%. Two (5.2%) urinary tract infections were reported. No cytomegalovirus or BK Polyomavirus infection was reported. The median serum creatinine at 1-year of follow-up was 1.1(0.8-1.3) mg/dI.

Conclusion: Our report, implies that ABOiKTx in post-COVID-19 candidates can be successfully performed with no major deviation from standard ABO protocol.
A Single-Center Analysis of Kidney Transplant Patients With COVID-19 Compared to Waitlisted in the Two Waves: An Indian Report With Future Implications for the Potential Next Wave

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Introduction: There is a paucity of data confronting the outcomes of COVID-19 in waitlisted compared to kidney transplant recipients from the developing world.

Methods: This was a retrospective cohort study of 334 hospitalized COVID-19 patients [waitlisted (n = 147) and KTR (n=187)] in a single center from India during two time periods of 5 May 20 to 23 September (first wave) and 26 March to 6 June 2021 (second wave). We aimed to compare the demographic, clinical profile, laboratory features, outcomes and risk factors.

Results: Among the demographic characteristics, waitlisted group had older age [45(35-54) vs 40(32-48); p-value < 0.01] and equal gender distribution (56.4% vs 81.8%; p-value < 0.01) compared to kidney transplant recipients. Overall, waitlisted patients were more symptomatic. The unadjusted 60-day mortality remained same across both the pandemic waves (log rank test, p-value = 0.9) but was higher for waitlisted patients (30.6% vs 17%; log rank test, p-value = 0.007). In a univariable analysis age more than 60 years, waitlist status, hypertension, diabetes, obesity was associated significant mortality. In a multivariate analysis, age (OR = 5.7(2.3-14); p-value < 0.01), hypertension (OR = 11(4.1-28); p-value < 0.01) and diabetes (OR = 2.3(1.1-5); p-value = 0.02) was associated with mortality. In multivariate analysis for prediction of severe disease, only hypertensive cases (OR = 4.8(2.2-10.5; p-value < 0.01) was found having association.

Conclusion: Our report describes greater mortality in waitlisted patients which is mostly contributed to a higher burden of co-morbidities in this population.
The COVID-19 Pandemic Has More Severely Affected Heart And Kidney Transplantation in Less-Developed Countries Compared to More Developed Countries

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Introduction: The COVID-19 pandemic has affected all aspects of human conditions of all nations, but some nations such as Brazil, India the United States had suffered disproportionately in terms of the total number of COVID-19 cases and COVID-19-related deaths. We investigated how the COVID-19 pandemic affected the transplantation of vital organs such as hearts and dispensable organs such as kidneys. We also investigated how the pandemic affected transplantation of these organs in developed countries where illegal kidney trading is absent, and in less developed countries including countries where illegal kidney trading had been reported.

Methods: Data on heart and kidney transplantation and per capita GDP in 2015-2020 were obtained from the Global Observatory on Donation and Transplantation (GODT) database and the World Trend Plus database, respectively. The effects of COVID-19 were tested using exploratory data analysis and nonparametric significance test using Wilcoxon Signed Rank test. The outcomes for 2020 were predicted using the Neural Network forecasting method and the predicted outcomes were compared with actual cases using the nonparametric method and Wilcoxon Signed Rank test. A p-value <0.05 was considered statistically significant.

Results: The countries were clustered based on per capita GDP into three groups (Group 1: Australia, Denmark, Norway, Sweden, Switzerland, and United States; Group 2: Belgium, Finland, France, Germany, Hong Kong, Israel, Italy, Japan, Kuwait, Slovenia, South Korea, and the United Kingdom; and Group 3: Argentina, Belarus, Brazil, Bulgaria, China, Croatia, Iran, Mexico, Pakistan, Romania, Russia, and Turkey). COVID-19 has negatively affected the transplantation of both vital and dispensable organs. For hearts, the effect is statistically significant in group 2 and countries but nonsignificant in Group 1 countries. For deceased kidneys, the effect is statistically significant in group 2 and 3 countries, but nonsignificant in Group 1 countries. For live donor kidneys, the effect is statistically significant in group 1 and 3 countries but not significant in Group 2 countries. For kidneys from both sources, the effect is statistically significant in group 3 countries, but nonsignificant in Group 1 and 2 countries.

Conclusions: Overall, the COVID-19 pandemic has more severely affected transplantation medicine in less developed countries compared to developed countries. Multiple factors, including health care infrastructures and overall national response to the COVID-19 pandemic, might have affected transplantation medicine during the COVID-19 pandemic. Further analyses of the impacts of COVID-19 can be helpful for preparedness in confronting future pandemics and reducing the impacts of the pandemics on healthcare including transplantation medicine.

Comparison of influenza and Covid-19 infections in solid organ transplant recipients

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Introduction: Respiratory viruses can occur with endemics and pandemics worldwide, which cause high morbidity and mortality in solid organ transplant (SOT) recipients. In this study we aim to evaluate the differences between two respiratory viruses (Influenza and SARS-CoV-2) in SOT recipients.

Method: In the study was compared SOT patients diagnosed with Influenza by PCR test between 2018-2020 and diagnosed with COVID-19 by PCR test between 2020-2022. Clinical characteristics and clinical course of two respiratory viruses were evaluated. The data of the patients were obtained from the hospital information management system and was analyzed with the SPSS programmes.

Results: There were a total of 95 patients. Fifty-three-three patients were diagnosed with COVID-19 and 42 patients diagnosed with Influenza. The median age was 49 (range 20-72) years for patients with COVID-19 and 47.5 (range 18-80) years for patients with Influenza. Male gender was higher than females in all cohort (71.6%). At admission 49.1% of patients with COVID-19 reported fever, 39.6% reported cough, 9.4% reported sore throat. The 71.4% of patients with Influenza reported fever, 57.1% reported cough and 31% reported sore throat. Fever and sore throat was significantly higher in Influenza group (p: 0.028, 0.008 respectively). Thorax computed tomography (CT) was performed 84.9% (p<0.001) patients in COVID-19 group, and 86.7% of them had any sign in CT (p: 0.003). While there was no significant difference in hospitalization between the groups, the need for intensive care support (32.1%) and mechanical ventilation (26.4%) was significantly higher in the COVID-19 group (p: 0.009, 0.005 respectively). Despite the fact that there was no significant difference, the duration of hospitalization and intensive care unit was longer in the COVID-19 group. The 90-days mortality rate was significantly higher in the COVID-19 group (13/53 (24.5%), p: 0.009).

Conclusion: Although solid organ transplantation can save lives, there is an increased risk of infection. Respiratory viral infections are among the most common infections, causing significant morbidity and mortality. Based on our results, COVID-19 have devastating effects as pulmonary involvement, ICU support, and higher mortality in SOT recipients than Influenza. Due to the ongoing pandemic and changing SARS-CoV-2 variants and effects, SOT patients should not neglect non-pharmaceutical interventions and their primary or booster vaccines.
315.1

5-HT2 and 5-HT2B Receptor Antagonism Abrogates Fibrotic Potential of Human Renal Allograft Fibroblasts by Targeting STAT3 Pathway

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Introduction: Despite improvements in immunosuppressive therapy, long-term allograft survival after kidney transplantation remains as low as 50%. The primary cause of chronic allograft nephropathy is “interstitial fibrosis and tubular atrophy” (IF/TA). Serotonin (5-HT; 5-Hydroxytryptamine) produces extracellular matrix proteins in presence of TGF-β1 dependent manner. TGF-β1 activates resident fibroblasts, trans-differentiate into myo-fibroblasts, which is the hallmark of the pathogenesis of fibrosis. We aimed to evaluate the anti-fibrotic role of inhibitors of 5-HT and 5-HT (Terguride and SB204741), respectively in human renal fibroblasts (HRFB) isolated from renal allograft rejection patients.

Methods: Renal fibroblasts isolated from renal allograft rejection patients (n=6) and controls (n=3), were incubated with 5-HT (1μM)/TGF-β1 (10ng/ml) for 1 hour and later with 5-HT (1μM)/TGF-β1 (10ng/ml) and terguride or SB204741 (1μM, each) for 24 hours (Post-treatment strategy). In the pre-treatment strategy, cells were pre-treated with terguride or SB204741 (1μM, each) for 1 hour and later with only 5-HT (1μM)/TGF-β1 (10ng/ml) for 24 hours. Real-time PCR for pro-fibrotic (TGFβ1, COL1A1, COL1A2, ACTA2, αSMA, and TIMP1) expression was performed. Type I collagen and α-SMA, the phosphorylation status of Smad3-3, ERK1/2, Src and STAT-3 was examined by western blotting.

Results: In 5-HT/TGF-β1 stimulated HRFB, upregulated pro-fibrotic gene expression was observed, which significantly reduced on co-culture with 5-HT/5-HT inhibitors, with no effect on anti-fibrotic genes mRNA expression (Figure 1). In 5-HT stimulated HRFB, treatment with both 5-HT inhibitors decreased type I collagen and α-SMA with reduced ERK1/2 phosphorylation, however, Smad3-3 phosphorylation remains unaltered. In 5-HT/TGF-β1 stimulated HRFB, 5-HT inhibitors decreased STAT3 phosphorylation, without affecting Src phosphorylation.

Conclusion: TGF-β1 mediated non-canonical pathways, ERK1/2 and STAT3 have been implicated in the development of fibrosis. 5-HT receptor antagonists might reduce the fibrotic potential of HRFB via suppression of TGF-β1 mediated non-canonical pathways.

315.2

Generation and Expansion of Functionally Stable Allospecific Tregs for Immunotherapy in Human Kidney Transplantation

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Although growing evidence demonstrates the feasibility of using allospecific T reg-based immunotherapy for transplantation tolerance, there is still little knowledge about Treg long term stability and functionality in vivo. Our group has established several methods for generating large numbers of allospecific tTregs, iTregs and Tr1, which preserve their suppressive phenotype and function in the presence of pro-inflammatory cytokines. Allo- tTregs, iTregs or Tr1 were obtained after in vitro stimulation with allogeneic monocyte-derived DCS or DC10 (for Tr1), they were FACS-sorted to a purity >95% and then, polyclonally expanded for 4-6 weeks. For thymic Tregs, alloTregs were expanded up to 2,300 times the initial numbers with a purity of >95% (CD4+CD25hiFOXP3+). The resulting allospecific Tregs showed high expression of CTLA-4, LAG-3, and CD39. Expanded thymic alloTregs efficiently suppressed T-cell proliferation in an antigen-specific manner, even in the presence of IFN-γ, IL-4, IL-6, or TNF-α. In the case of alloantigen-induced Foxp3+ Tregs, they were also polyclonally expanded for 6 weeks in the presence of TGF-β1, IL-2, and rapamycin, giving rise to 4,600 million Tregs (230,000 x). Finally, Tr1 cells CD49b+ LAG-3 (<80%), where generated, which produced high levels of IL-10 (≈90%) and expressed co-inhibitory receptors (PD-1, CTLA-4, TIM-3, TIGIT, CD39), as well as chemokine receptors CCR2, CCR4 and CXCR3. Most importantly tTregs, iTregs and Tr1 specifically suppressed allospecific, but not third party, T cell proliferation, in the presence of pro-inflammatory cytokines. Our data indicate that expanded-allo-Tregs are stable and express relevant chemokine receptors, suggestive of their potential homing to the kidney allograft.

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Targeted Delivery of Galunisertib Attenuates Fibrogenesis in an Integrated Ex Vivo Renal Transplant and Fibrosis Model

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Background: Normothermic machine perfusion (NMP) is an emerging preservation technique for kidney allografts to reduce post-transplant complications, including interstitial fibrosis and tubular atrophy. This technique could be improved by adding antifibrotic molecules to perfusion solutions. We introduce a novel therapeutic approach, tested in a newly developed fibrosis model, to suppress fibrogenesis entitled Machine perfusion and Organ slices as a Platform for Ex vivo Drug delivery (MOPED). Our approach involves ex vivo perfusion with a blood based perfusate spiked with transforming growth factor beta (TGF-β) —one of the most important cytokines involved in fibrogenesis—and added galunisertib—a potent inhibitor of the TGF-β signalling pathway.

Methods: Porcine kidneys were subjected to 30min of warm ischemia, 24h of oxygenated hypothermic machine perfusion (HMP), and 6h of NMP with treatment (control, TGF-β, galunisertib, or TGF-β+galunisertib; n=8). To determine whether effects persisted upon ceasing treatment, precision-cut kidney slices (PCKS) were prepared from respective kidneys and incubated for 48h with treatment continued and discontinued (Figure 1a).

Results: Galunisertib supplementation improved the general viability, characterized by an increased oxygen consumption, elevated ATP levels and attenuated tubular dilation and necrosis. No significant differences in renal function, oxidative stress levels, or injury markers were observed. Galunisertib altered inflammation markers by causing a significant increase in gene expression of TNF-α, and a significant decrease of IL-6 after 6h NMP. This was supported by IL-6 protein expression. Continued TGF-β supplementation promoted fibrogenesis as shown by significantly increased mRNA expression of ACTA2, COL1A2, FN-1, SERPINE1, SERPINH1, and TGF-β after 48h of incubation. Continued treatment with galunisertib, however, clearly attenuated the expression of all tested fibrosis-related genes after 48h incubation (Figure 1b-g).

Conclusions: Our findings suggest that galunisertib positively affected mitochondrial activity, tissue integrity and expression of fibrogenesis-related genes, and therefore appears to be a promising drug for further research. These findings illustrate the value of targeted drug delivery using isolated organ perfusion for reducing post-transplant complications.

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315.4

CREB May Regulate Gene Expression in MDSC Differentiation by Influencing DNA Methylation

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Introduction: As an immunosuppressive cell, myeloid-derived suppressor cells (MDSC) has been reported to play a positive role in kidney transplantation. ATF/cyclic AMP-responsive element-binding (CREB), as a transcription factor, has been reported in macrophages with PGE2 addition. Hypermethylated MDSC induced by PGE2 are also myeloid-origin cells. There have been no reports on whether CREB also plays a regulatory role in this differentiation process.

Method: Bone marrow (BM) cells of C57BL/6 were used to induced MDSC with GM-CSF (20ng/mL) and PGE2(1μg/mL) or with GM-CSF (20ng/mL) and EP1/2/4 antagonists. The expression of CREB, DUSP2 and MYD88 were assessed. The methylation level of their promoter region was measured using BSPCR. CREB inhibitor was used to study its effects.

Results: In hypermethylated MDSC induced by GM-CSF and PGE2 and bone marrow cells induced by GM-CSF and EP1/2/4 antagonists, CREB was found in both of them. Meanwhile, two other proteins, DUSP2 and MYD88, which had been reported to be elevated in LPS-stimulated macrophages and did not decrease after the addition of PGE2, were also increased in MDSC compared with cultured BM cells. After adding CREB inhibitor (KG-501) to the hypermethylated MDSC culture system, we tested the expression of these two proteins again. The expression levels of both proteins were reduced. The methylation level of the promoter region of the two was higher than that of the group without CREB inhibitor. The DNA methyltransferase 3 Alpha (Dnmt3α) was not found any difference with or without inhibitor.

Conclusion: In hypermethylated MDSC induced by GM-CSF and PGE2 and bone marrow cells induced by GM-CSF and EP1/2/4 antagonists, CREB is involved in the regulation of DUSP2 and MYD88, possibly by competing with Dnmt3a on DNA binding in the regulation of promoter methylation. This is the first study focusing on the relation between CREB and DNA methylation by Dnmt3a.

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315.5

Mesenchymal Stromal Cell Therapy as a Promising Option To Increase Organ Availability and Reduce Graft Failure

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Aim: The aim of the current study is to evaluate the effect of MSCs administered to aspiration damaged lungs during ex vivo lung perfusion (EVLP) and to recipients post transplantation with a focus on their capacity to improve lung function in treated recipients compared to both waiting list mortality and post-operative complications such as primary graft dysfunction (PGD). Although donor numbers increase, donor organ utility is low due to acute lung injury (ALI) which can be induced by gastric aspiration. Mesenchymal stromal cells (MSCs) have caught attention for organ regeneration as they display an array of potentially beneficial effects: they are known to be immunomodulatory, antifibrotic and microbiocidal. MSCs have demonstrated tissue regenerative capacities as documented in preclinical studies, e.g., improved function of diseased lungs.

Introduction: Lung transplantation (LTx) is an established therapeutic option for end-stage pulmonary disease. However, waiting lists are long and the treatments remains hampered by donor lung scarcity accompanied with high early and late mortality rates. Novel treatment options to regenerate marginal donor lungs turned down for transplant are needed to combat both waiting list mortality and post-operative complications such as primary graft dysfunction (PGD). Although donor numbers increase, donor organ utility is low due to acute lung injury (ALI) which can be induced by gastric aspiration. Mesenchymal stromal cells (MSCs) have caught attention for organ regeneration as they display an array of potentially beneficial effects: they are known to be immunomodulatory, antifibrotic and microbiocidal. MSCs have demonstrated tissue regenerative capacities as documented in preclinical studies, e.g., improved function of diseased lungs.

Materials and Methods: Lung injury was induced in 12 donor pigs using gastric content with a pH of 2. The donor-recipient pairs were randomized to receive MSCs or placebo treatment during the beginning of EVLP and post LTx. Lungs were treated with EVLP for 4 hours followed by a left lung transplantation. The recipient was kept under anesthesia and closely monitored for three days post LTx. In the final phase of the experimental setup an isolated assessment of the transplanted lung was achieved following a right pneumonectomy. Treatment effects were assessed by clinically relevant parameters, including PaO2/FiO2 ratio, pulmonary vascular resistance (PVR), and lactate, further by histopathological changes, immune cell counts in peripheral blood and cytokine and chemokine levels in plasma and bronchoalveolar lavage fluid during the course of the experiment.

Results: The lung functionality as evaluated by the PaO2/FiO2 ratios showed significantly increased lung function in treated recipients compared to both the non-treated recipient and to all lungs at the time of confirmed ALI. A tendency of higher PVR was seen among the non-treated recipients however, not significantly. Lactate was unchanged in both groups. Lung injury scores were also reduced in the treated group as compared to the non-treated group and to the lungs after lung injury was induced. On the third day of follow-up of the recipients, all recipients in the treatment group had PGD grade 0, while the non-treated group consisted of one recipient with grade 0, three with grade 2 and two with grade 3.

Conclusion: MSC treatment emerges as a promising therapeutic option for restoring injured donor lungs for reacceptance into the donor pool and decreasing the incidence of PGD.
Assessment of Biliary Regeneration During Long Term (>5 Days) Ex-vivo Normothermic Machine Perfusion

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Introduction: Biliary strictures after liver transplantation are hypothesised to result from an imbalance between biliary injury and biliary regeneration. Evaluation of biliary regeneration could, in theory, identify grafts likely to develop a biliary stricture. Assessment of biliary regeneration before transplantation is currently not possible due the 24-hour delay in cholangiocyte proliferation. We have developed a method of long-term ex-vivo normothermic machine perfusion (NMP) that could support grafts beyond 24 hours. This study was performed to investigate biliary regeneration during long-term ex-vivo NMP.

Methods: Human livers unsuitable for transplantation were perfused at normothermia beyond 24 hours. Long-term perfusion was achieved using a modified commercial system including dialysis, hormonal and nutritional support. Serial biopsies of the bile duct were collected throughout perfusion for histopathology. Biopsies were examined for presence of biliary epithelium and compared between time-points. Bile biochemistry was also measured.

Results: Eleven grafts were evaluated using long-term NMP up to 13 days. Grafts were unsuitable for transplantation due to medically unsuitable donor (n=2), steatosis (n=2) and donation after circulatory death (n=7). Eight grafts (88%) had complete biliary epithelial loss within 24 hours reperfusion. By 144 hours perfusion, biliary epithelium was identified in seven grafts (88%) suggesting re-epithelisation. Presence of epithelium was not correlated with bile pH or glucose.

Conclusions: This is the first study to demonstrate biliary regeneration after 24 hours of NMP. Long-term NMP has the potential to assess biliary regeneration and identify grafts likely to develop biliary stricture after transplant. Additional biomarkers for biliary regeneration are being investigated.
The Molecular Nature of the Banff iIFTA Lesion

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Introduction: Inflammation within areas of interstitial fibrosis and tubular atrophy (iIFTA) have been linked to adverse outcomes in kidney transplantation through an association with T-cell immunity leading to altered renal parenchymal structures. To date there is no literature that describes changes in the transcriptome in transplant recipients with iIFTA lesions. Further, molecular evidence for the progression of the banff iIFTA lesion, within the first year of transplantation, remains absent from the literature. Herein we define molecular changes within kidney allografts with an iIFTA lesion. We further characterise molecular signatures that accurately describe the progression of iIFTA at 12-months on a 3-month protocol biopsy.

Methods: We performed RNA sequencing of 113 protocol biopsies with all samples scored by the same histopathologist. Differentially expressed genes were deemed significant if they had a Benjamini-Hochberg adjusted P < 0.05. We then performed a gene set enrichment analysis using the gene ontology database to identify biological pathways that were enriched in iIFTA lesions. We also compared the transcriptomic profiles of patients with antibody- and T-cell mediated rejection with the iIFTA lesion. We further interrogated the same cohort for the progression of their iIFTA score at 12-months. Differential gene expression, and pathway analysis were employed to identify risk genes in patients that developed high iIFTA at 12-months post-transplant.

Results: Of the 113 biopsies with RNA sequencing, 37 demonstrated iIFTA by histopathology. Following transcriptomic analysis, 336 genes were differentially expressed in biopsies with an iIFTA diagnosis. The top ranking genes and pathways were all involved in the formation of immunoglobin and B-cell activation. Further, transcriptomic changes in the iIFTA lesion closely resembled those found in antibody-mediated rejection. Finally, we demonstrate that genomic information, from both peripheral blood and kidney biopsy 3-months post-transplant, provides better prediction power than clinical data in identifying patients with iIFTA lesions.

Conclusion: RNA sequencing enabled us to identify novel transcriptomic changes in patients with iIFTA. This pathology is primarily driven by immune-based changes, closely resembling antibody-mediated rejection, which is at odds with the current concept of iIFTA mediated by T-cell activation. Further, this study aims to build a foundation for using molecular technology in identifying the progression of the Banff iIFTA lesion.
Single Cell RNA Sequencing of Cryopreserved Human Renal Transplant Core Biopsies: A Feasibility and Optimisation Study

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Background: Single cell RNA sequencing (scRNAseq) of tissue infiltrating leukocytes within human kidney transplants presents several technical challenges. For example, dissociation protocols may cause cell death or transcriptomic skewing, whilst creating single cell suspensions from freshly acquired biopsies is often impractical.

Aims: 1) compare and optimise leukocyte yield from three dissociation protocols and 2) evaluate the feasibility of scRNAseq on leukocytes from cryopreserved human kidney transplant biopsies.

Methods: Three digestion protocols (cold, warm manual, and warm automated enzymatic digestion) were evaluated using core biopsies from porcine kidney to optimise dissociation protocols. Following this, renal biopsies were taken from two patients at 5- and 9-months following transplant and dissociated into single cell suspensions by warm manual enzymatic digestion, which were then flow sorted to isolate CD45+ cells. cDNA libraries were produced with either 3’ or 5’ gene expression (GEX) kits from 10x Genomics and sequenced by Illumina NextSeq. Reads were aligned to the reference transcriptome GRCh38 (CellRanger) with QC, normalisation (SCTransform), clustering, and annotation performed with Seurat and SingleR.

Results: Warm manual enzymatic digestion was found to be the superior method for dissociation. With warm manual enzymatic digestion, a mean of 3906 (2512—6045) live CD45+ cells were isolated. Libraries were successfully generated for two biopsies: the 5-month biopsy from the first patient using the 3’ GEX preparation protocol; and the 9-month biopsy from the second patient using the 5’ GEX protocol. Following QC, a total of 12475 RNA transcripts in 396 cells, and 13128 RNA transcripts in 699 cells were identified in the 5-month and 9-month biopsy respectively. Clustering and automated annotation demonstrated that T cells, followed by NK cells, were the most abundant cell types identified. Of the top 20 highly variable genes, 6 were common to both samples (GNLY, HLA-DRA, CCL4, GZMB, CST3, and AIF1). Allograft Inflammatory Factor 1 (AIF1) has previously been identified as a marker of chronic rejection and vascular inflammation whilst Cystatin 3 (CST3) is a biomarker of kidney function. Expression of both these genes localised specifically to the monocyte/macrophage cluster within both samples.

Discussion: Here we successfully characterise the leukocyte transcriptome within cryopreserved human kidney core biopsies. We identify an inflammatory monocyte/macrophage signature within samples dissociated by this protocol. Whether this is biological or technical remains to be determined, particularly as both patients maintain stable transplant function. Nevertheless, we demonstrate that scRNAseq from cryopreserved human transplant biopsies is feasible and enables deep transcriptomic analysis of tissue-infiltrating immune populations.

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Gene Expression Patterns After 2 Hours of Normothermic Ex-vivo Kidney Perfusion Potentially Predict Occurrence of Future Acute Rejection: A Preliminary Analysis

Introduction: Normothermic ex-vivo kidney perfusion (NEVKP) prior to kidney transplantation recreates a near-physiological environment, recon-ditioning the organ and allowing superior assessment of organ quality. The impact of this technology has yet to be exploited and might be significant for the use of marginal donor kidneys due to the potential for viability assessment. In this study, we aimed at investigating gene expression patterns of marginal donor kidneys undergoing 2 additional hours of NEVKP after hypothermic machine perfusion (HMP)/static cold storage (SCS) prior to transplantation.

Method: Eleven marginal donor kidneys included in this study were preserved under HMP (n = 8) or SCS (n = 3) after retrieval and subsequently underwent 2 hours of end-ischemic NEVKP prior to transplantation. During NEVKP, kidney biopsy samples were collected at the beginning of the procedure, after 1 h of perfusion, and after 2 h of perfusion. The biopsies were formalin-fixed paraffin-embedded (FFPE). Gene expression patterns were investigated using the NanoString® Banff-Human Organ Transplant Panel. Data were analyzed using the NanoString nSolver® Advanced Analysis module.

Results: Eleven kidney transplant recipients were initially included in this prospective study. For the current analysis, two patients did not have sufficient FFPE material for RNA assessment and were therefore excluded. Four transplant recipients were diagnosed with acute rejection within the first three months after transplantation while the other five showed stable graft function. Two distinct sample clusters based on gene expression patterns related to the development of an acute rejection episode within the first 3 months after transplantation could be identified after 2 h of NEVKP (Fig. 1-2). Genes that, among other functions, are known to take part in immune regulation and apoptosis pathways (i.e. STAT6, BCL2, IKBKG, SOCS1, AXL, RASIP1, TRAF4, CIITA, IKBKG, VEGFA, vCAM) appeared to be differentially, however not significantly (p < 0.05, q > 0.05), expressed at 2 h of NEVKP in transplants that subsequently developed acute rejection compared to those maintaining a stable graft function. Moreover, promising trends in multiple molecular pathway scores were found, including apoptosis, autophagy, oxidative stress, and the inflammasome.

Conclusion: NEVKP elicits different gene expression patterns between marginal kidneys that will successively develop acute rejection and those maintaining a stable graft function within the first three months following kidney transplantation. A higher expression of genes related to apoptosis might indicate a greater extent of cellular damage in the perfused graft, increasing antigen presentation and therefore the likelihood of acute rejection. The potential to predict acute rejection occurrence before transplantation will allow for a more tailored therapeutic management in order to improve kidney transplant outcome and recipient quality of life.

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Tacrolimus Withdrawal After Mesenchymal Stromal Cell Therapy Is Associated With Donor-Specific Antibody Formation in Kidney Transplant Recipients

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Introduction: Recently, the clinical phase II Triton study demonstrated that mesenchymal stromal cell (MSC) therapy is a safe method to facilitate tacrolimus withdrawal in kidney transplant recipients (KTRs). Here, we analyzed de novo donor-specific antibody (dnDSA) formation and HLA molecular mismatch in MSC-treated KTRs.

Methods: All patients underwent a first, living-donor kidney transplantation and received alemtuzumab induction, steroids, tacrolimus and everolimus. Patients in the MSC arm of the study received two infusions of autologous MSC at week 6 and 7 post-transplantation. Subsequently, tacrolimus was tapered and completely withdrawn at week 8. Patient sera were tested by luminex single antigen bead (SAB) assays (Immucor) for dnDSA assignment; positivity was defined as MPI > 1000. DSA were further characterized using a modified SAB assay to detect IgG1, IgG2, IgG3 and IgG4 subclasses. Complement binding was assessed with a C3d assay (Immucor). Patients and donors were HLA typed on 11 loci by next-generation sequencing. Eplet mismatches were calculated using HLAMatchmaker 2.0.

Results: In total, 3 out of 27 patients (11%) in the control group and 11 out of 29 patients (38%) in the MSC group developed dnDSA, of which the majority was directed against HLA-DQ. The majority of DSA were complement binding and had different IgG subclasses. Although patients in the MSC group had an increased rate of dnDSA formation, the degree of antigen mismatch was similar to the control group (Figure 1). Cox regression showed that both MSC treatment group (HR=2.474, P=0.032) and HLA class II antibody-verified eplet mismatch (HR=1.176 per single eplet mismatch, P=0.001) were independently associated with dnDSA development. Despite the increased dnDSA formation in MSC-treated patients, incidence of rejection or graft loss was not increased and eGFR was stable at 2 years follow-up (Figure 2).

Conclusion: Tacrolimus withdrawal after MSC therapy is associated with an increased rate of dnDSA formation in KTRs. However, no increased risk of rejection or inferior graft function was found, raising the question on the pathogenicity of these DSA, despite the presence of complement fixing IgG subclasses. We found that patients with a high HLA class II eplet mismatch load were less likely to tolerate tacrolimus withdrawal without developing dnDSA, which is in line with previous findings that HLA eplet mismatch load modifies tacrolimus through levels required to prevent dnDSA formation. Further research is warranted to explore HLA molecular mismatch load as a biomarker to guide personalized immunosuppression in transplantation.

Jon J van Rood Transplantatiefonds.

Repeated Mesenchymal Stromal Cell Therapy Repaired ARDS-damaged Donor Lungs and Reduces Primary Graft Dysfunction Following Lung Transplantation

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Purpose: Lung transplantation faces two unresolved challenges: the inadequate number of transplantable donor organs and the low survival rate in recipients who do receive a graft. Consequently, the waitlist mortality rate is high, and the 5-year survival for recipients remains less than 50%. Nevertheless, research in this field has yet to identify a therapy that addresses either problem. As mesenchymal stromal (stem) cells (MSCs) emerge as a promising tool in other lung-related diseases, mesenchymal stromal cells administered during ex vivo lung perfusion (EVLIP) and post transplantation at two timepoints were studied under the hypothesis that the therapy could improve damaged lungs and reduce the incidence of PGD.

Methods: Acute respiratory distress syndrome (ARDS) was induced using E. coli-derived lipopolysaccharide in donor pigs, and confirmed via blood gas values, chest x-ray and histology. Harvested lungs were placed on EVLP for 4 hours, and the left lungs were transplanted. Recipients were followed and closely monitored over 3 days. At the 3rd day a right pneumectomy was done and the transplanted left lung alone was evaluated over 4 hours. The treatment group consisted of six donor lungs which received intravascular doses of MSCs during EVLP and at 2 timepoints following transplantation. 6 lungs were maintained as a non-treated group which underwent the same protocol.

Results: Histological assessment based on blinded lung injury scoring of 7 parameters demonstrated that the treated lungs were significantly less injured both after EVLP and after transplantation than the non-treated ones and significantly less than biopsies taken at the time of confirmed ARDS. Assessment of lung functionality through the PaO2/FiO2 ratio showed that treated recipients had ratios significantly increased compared at the time of confirmed ARDS and to the transplanted non-treated recipients. All six of the treated group were PGH grade 0 on the third day of follow-up, while the non-treated group consisted of one grade 2 and five grade 3 recipients. Cell counts of leukocytes were comparable in plasma at the induction of ARDS and in the perfusate during EVLP, however, lymphocytes were significantly decreased in the treated group relative to the non-treated during the first day following transplantation.

Conclusion: Repeated mesenchymal stromal cell therapy at both EVLP and early during the post-transplantation period enabled repair of lungs with ARDS and decreased the incidence of PGD. Theamelioration of lung function by MSCs shows potential clinical use to increase the donor lung pool for lung transplantation and reduce PGD.
Gender Disparities in Renal Replacement Therapies in Colombia

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Introduction: In chronic kidney disease (CKD) there are historical inequities in multiple stages of the pathway for organ transplantation: access to waiting lists, organ distribution of deceased donor kidneys, living donor kidney transplant recipients, and preemptive transplantation. Non-medical factors that can affect access to transplants include gender inequity in which men are favored. Women have been recognized as disadvantaged within this process even after several efforts. This inequity has been repeatedly proven through data analysis of the US databases. In Colombia, there is a gendered difference in access to waiting lists, kidney allocation of cadaveric donors, and living donor recipients; although this has never been analyzed from information published by a local entity in Colombia.

Methods: Cross-sectional study based on secondary analysis of local public information between 2015 and 2020, which includes chronic kidney disease, chronic hypertension, and diabetes, waiting list, deceased and living donor transplantation. Healthcare professionals in transplantation were also analyzed.

Results: In Colombia, 4,934,914 patients were diagnosed with hypertension, diabetes or chronic kidney disease. 60.64% were female, with a mean age 63.84 years old (SD 14.36 years). Crude incidence for hypertension was 8.34 cases/100,000 inhabitants and crude prevalence was 9.02 cases/100,000 inhabitants, being higher for females. CKD incidence was 3.85 for female and 2.98 for males. Mortality for diabetic patients was 7.21/100 inhabitants. Diabetes mellitus' crude incidence was 3.77 cases/100,000 inhabitants, there were more females with hypertension than males (10.85 vs 7.21/100 inhabitants); Diabetes mellitus' crude incidence was 3.77 for female and 2.79 for male/1000 inhabitants. Mortality is similar for both genders. Crude incidence for renal replacement therapy was 86.45 cases/100,000 inhabitants. Waiting list by 2020 had 3003 patients nationwide, 56.3% male and 43.7% female. There were 251 deaths while on waiting list, 38% female. By 2020 a total of 797 kidney transplants were performed, 42% were female. Kidney transplant incidence was 11.95 cases/100,000 inhabitants. Waiting list by 2020 had 3003 patients nationwide, 56.3% male and 43.7% female. There were 251 deaths while on waiting list, 38% female. By 2020 a total of 797 kidney transplants were performed, 42% were female. Kidney transplant incidence was 11.95/1000 000 inhabitants.

Conclusion: In Colombia according to national records, there are proportionally more females with ESRD, nevertheless there are less females in waiting list and transplanted annually. This may represent diverse barriers which should be identified and addressed accordingly in order to improve female access to renal replacement therapy.

The Stem Cell Mobilizer Plerixafor Reduces Transplant Vasculopathy in a Murine Aortic Allograft Model

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Purpose: Effector and regulatory T cells (Tregs) are main cell populations in the context of cardiac allograft vasculopathy (CAV). The immunostimulant plerixafor mobilizes hematopoietic stem cells and may boost T cell. Therefore, the aim of this study was to evaluate if a single or repeated application as well as continuous treatment with plerixafor increases peripheral bone marrow derived stem cells including Tregs leading to tolerance induction and thus reducing chronic rejection in a mouse allograft transplant model.

Methods: Fully allogeneic mouse aortas from C57BL/6 mice (H2b) were abdominally transplanted into CBA mice (H2k). The continuous plerixafor application [1mg/kg/d] was carried out for 14 days using implanted small osmotic pumps. Single dose (s.c.) injection of 1mg/kg/d or 5mg/kg/d were done at day 1 after transplantation (Tx.) and pulsed injections [1mg/kg/d] were conducted on days 1, 7, 14, and 21 after Tx. The control allograft group received vehicle loaded osmotic pumps. Stem cell mobilization was monitored by FACS. Recipients were sacrificed on day 14 for intragraft gene expression analysis or on day 30 for histological measurements.

Results: Murine aortic grafts with puls ed plerixafor injections showed significantly reduced neointima proliferation compared to control allografts (33.65±8.84% vs. 53.13% ±12.41%; p<0.05). The single shot and continuous treatment groups exhibited no improvement concerning neointima formation vs. the untreated group. First FACS analysis revealed significantly less hematopoietic stem cells (HSC) in the bone marrow of plerixafor treated mice vs. the control at day 14 after Tx. Though, there were significantly more HSCs in the peripheral blood on day 30 after Tx, with the pulsed injection even doubling HSCs [0.0152%±0.008% p < 0.005 (pulsed); 0.0046%±0.002%; p < 0.01 (pump); 0.0076%±0.001%; p < 0.01 (single dose of 1mg/kg); 0.0039%±0.0017%; p < 0.1 (single dose of 5mg/kg) vs. 0.0018%±0.0016% (control)]. Intragraft gene expression results showed clearly reduced IFNγ expression and a significantly increase of IL-4, IL-10 and TGFβ.

Conclusion: The data suggests that pulsed, continued and single dose application of plerixafor leads to potent stem cell mobilization and hereby the repeated treatment with plerixafor reduces neointima formation in a mouse aortic transplant model.

Manfred-Roth Stiftung, Forschungsstiftung Medizin, FAU Erlangen-Nürnberg.
Development of a Registry for Gender Equity Analysis (ASTREG-WIT-KT) in Asian-Pacific Countries

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Introduction: Gender inequity in kidney transplantation (KT) is a global issue but may be more evident in Asia than in Western countries because of social, cultural, and economic influences. In order to elucidate the reasons and define solutions and strategies to reduce and eliminate health disparities, we have established a web-based registry (ASTREG-WIT-KT) and analyzed data on proportions of female in kidney donation and transplantation from 6 Asian-Pacific countries.

Methods: An online registry was constructed using the platform of the Asian Transplantation Registry (ASTREG-WIT-KT, http://ecrf.astreg.org). We collected data (2015-2019) on 360 variables related to gender, ethnicity and other socioeconomic factors about kidney donation and transplantation, dialysis, waiting list, and chronic kidney disease from 6 Asian-Pacific countries of Australia, India, Japan, Korea, Philippines, and Taiwan and analyzed.

ASTREG-WIT-KT has been built as an online platform for collecting and visualizing gender-related statistics of kidney transplantation from aggregated national or institutional databases. Data are presented according to different years and countries and the trend over 5 years is analyzed with the joinpoint regression.

Results: We found that the proportion of female living donors was the highest in India (ranged from 72.3 to 81.1%) and the lowest in the Philippines (ranged from 37.5 to 41.6%). The proportion of female living donors was over 50% in all participating countries except the Philippines. Australia (annual percent change (APC) -1.5, p = 0.015) and Japan (APC -0.9, P = 0.024) showed decreasing trend of female living donors for five years. The proportion was the highest for female spousal donors. All participating countries showed less than 50% of female recipients received a living donor KT (LDKT). The proportion of female recipients who received a LDKT ranged from 21.5 to 50.0%. The proportion of female recipients in DDKT showed increasing trend in Australia (APC 1.8, P = 0.004). Proportions of females on the waiting list were less than 50% among all countries with available data.

Conclusion: ASTREG-WIT-KT is established to support collaborative studies on promoting gender equity in KT, especially in Asian-Pacific countries. Our preliminary data showed that gender inequity existed and persisted, showing large differences in female fractions for the living kidney donor and the recipient. A data-based approach for identifying both biological and social factors will be necessary for achieving gender equity in KT.


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Introduction: In transplantation, the endothelial lining is the first barrier between the donor organ and recipient immune system. Damaged endothelium exposes extracellular matrix (ECM) molecules that can trigger inflammation and cause graft rejection. Preservation and restoration of the endothelial barrier function is thus crucial for the normal performance of the kidney vascular system after transplantation. Here we prove that re-endothelialization of acellular blood vessels using patient derived kidney-vein endothelial cells (EC) restores both the vascular barrier function and innate immune function of the endothelium.

Methods: Human common iliac veins (CIV) (n=19) from deceased healthy donors were decellularized by submersion in Triton X-100 (4%), ammonia (1%) and DNase. Efficacy of the process was evaluated via histological analysis and quantification of DNA. The ECM protein makeup preservation was assessed via collagen and sGAG content. Decellularized CIV were subsequently repopulated with human umbilical vein endothelial cells (HUCVEC) or patient derived kidney-vein EC. The re-endothelialized veins were analysed using confocal microscopy for EC confluency. Functionality of the EC barrier was analyzed using trans-endothelial electrical resistance (TEER), dextran (4 and 70 kDa) permeability and nitric oxide production (eNOS). The innate immune barrier function of recellularized scaffolds was assessed by co-culture with THP-1 monocytes (8:1 ratio) in a home built transmigration system.

Results: The CIV were fully decellularized, demonstrated by the complete removal of cellular components, and the removal of dsDNA (before: 83.8±29.0, after:13.0±6.5 ng/mg). Histological integrity was preserved, as well as ECM polysaccharides and collagen. Confocal microscopy showed the formation of a confluent monolayer of cells as soon as 24 hours after seeding. After 28 days of culture repopulated CIV scaffolds remained confluent and cells expressed the proliferation marker Ki-67 and PECAM-1. At day 10, the constructs had TEER measurements above background of 15.1±12.2 Ω·cm² (n=4); reduced dextran permeability compared to decellularized CIV (2.3-fold for 4kDa and 4.7-fold for 70kDa; n=3); and showed higher nitrate and nitrite concentration compared to plastic cultures (n=4). These results indicated the restoration of a functional EC barrier. The innate immune barrier function was demonstrated by THP-1 cell adhesion (only on recellularized scaffolds) and transmigration through the EC monolayer. THP-1 differentiation into M1 inflammatory macrophages and M2 anti-inflammatory macrophages was confirmed via flow cytometry and immunohistochemistry with representative markers (CD14, CD16, CD80 and CD163).

Conclusion: We used an in-vitro ECM blood vessel model to prove functionality of recellularized human vein tissue with patient-derived kidney vein EC. Repopulated scaffolds also showed immune innate function, paving the way to future translation into clinical practice.
Incidence and Effect on Survival of Delayed Graft Function in Donor-Deceased Kidney Transplants in Argentina: A Multicenter Analysis

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Introduction: Delayed graft function (DGF) is a manifestation of acute kidney injury with attributes unique to the transplant process. DGF is associated with negative outcomes such as higher incidence of acute rejection, worse graft function and lower grafts and patients’ survival. Although the worldwide incidence of DGF is variable, a previous study showed that the incidence in Argentina is higher than the US and most countries in Europe. Therefore, the aim of our study was to identify the risk factors associated with DGF in Argentina and to evaluate the impact of DGF on grafts’ and patients’ survival.

Methods: Retrospective multicenter cohort study of deceased-donor kidney transplant from 33 transplant centers in Argentina between 2015 and 2017. Demographic data and donor and recipient related variables were analyzed at baseline and at 3 and 5 years of follow-up. Data were obtained from SINTRA/ INCUCAI, the Argentinian procurement organization and from the transplant centers.

Results: Between 2015 and 2017, 1886 single kidney transplants were performed in 33 centers. Recipient and donor characteristics are shown in Table 1. In the current study, the incidence of DGF was 62%. Univariate analysis demonstrated that higher donor creatinine, donor age, recipient time on dialysis, donor BMI, absence of induction and cold ischemia time were risk factors associated with DGF. Multiple organ donation and cause of death other than stroke were associated with reduced risk DGF. In the multivariable analysis donor age (P<0.02), higher donor creatinine (P<0.02), recipient time on dialysis (<0.01), cold ischemia time (<0.01), monorganic donor (<0.01)) were risk factors of DGF. Renal function was significantly better in patients without DGF throughout the 5 years follow-up (P<0.05). Patients with DGF had higher incidence of acute rejection in the first three months of follow-up, with T-cell mediated rejection being the most frequent. At 3 and 5 years of follow up there was no increased risk of rejection when both groups were compared. Graft survival and patient survival were lower in the group that developed DGF at 1, 3 and 5 years of follow-up (<0.01) (Figure 1).

Conclusion: We confirmed the high incidence of DGF in our country. Furthermore, the analysis on the risk factors associated with DGF were not as much different as in other countries where the incidence of DGF were lower. Further studies should be done to unravel the cause of this high incidence of DGF in Argentina.

316.2
Single-Center Experience With Acute Kidney Injury Deceased Donor Kidneys From Marginal Donors
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Introduction: Many centers will selectively transplant kidneys from standard criteria donors (SCD) with terminal acute kidney injury (AKI). However, there is limited experience with transplanting kidneys either from expanded criteria donors (ECD) or donation after cardiac death (DCD) deceased donors (DD) with terminal AKI and many of these organs may be discarded. The study purpose was to review retrospectively our experience with transplanting kidneys from "marginal" AKI DDs (MDDs).

Methods: AKI kidneys were defined by a doubling of the DD's admission serum creatinine (SCr) level and a terminal SCr level >2.0 mg/dl whereas MDD kidneys were defined as DCD or ECDs using UNOS definitions. Dual kidney and multi-organ transplant recipients were excluded. All patients received depleting antibody induction and triple maintenance therapy (FK, MPA, steroids).

Results: From 1/07 to 11/21, we transplanted 236 single AKI DD kidneys including 29 from ECDs/16 DCDs (n=45 MDDs) and 191 from SCDs. When comparing the 2 groups, mean donor age (47 MDD vs 33 years SCD), KDPI (72% MDD vs 45% SCD), and recipient age (59 MDD vs 50 years SCD) were lower in the SCD group. Mean terminal SCr level (2.8 MDD vs 3.2 mg/dl SCD) was higher in the SCD group but cold ischemic times (mean 24.4 hours) were comparable even though 56% of AKI MDD kidneys were imported from other donor service areas. 60% of patients had at least 5 years follow-up in both groups. The incidence of delayed graft function (DGF, dialysis in the first week) was 38% MDD vs 59% SCD (p=0.012) whereas the incidence of primary nonfunction (PNF) was 0 MDD vs 2.1% SCD (p=NS). One-year patient and kidney graft survival rates (GSR) were 98% vs 97% and 93% vs 93% (p=NS) in the MDD vs SCD groups, respectively. Mean 1-year SCr (1.7 MDD vs 1.5mg/dl SCD) and GFR (43 MDD vs 56ml/min/1.73 m2 SCD) levels suggested improved renal function with SCD kidneys. With a mean follow-up of 65 months in the MDD group, overall patient and kidney GSRs were 78% vs 75% (p=NS) and 73% vs 59% (p=0.088) in the MDD vs SCD groups, respectively. However, actual 5-year kidney GSRs were 68% MDD vs 75% SCD (p=NS).

Conclusion: In spite of diminished 1-year renal function, the use of kidneys from AKI DDs can be safely liberalized to include selected ECD and DCD donors without incurring a higher risk of DGF, PNF, or intermediate-term graft loss.

316.3
Influence of CIT-Induced DGF on Transplant Outcomes Among DCD Kidneys
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Background: Donation after circulatory death (DDC) kidneys are exposed to ischemic events from withdrawal of support, which when coupled with increased cold ischemia time (CIT) predisposes to delayed graft function (DGF). DGF is considered a risk factor for graft failure after kidney transplantation. Clinicians may be reluctant to transplant DCD kidneys that also have prolonged CIT for fear of an additional deleterious effect.

Methods: To analyze the risk of CIT-induced DGF on graft survival among DCD kidneys, we evaluated national data between 2008 and 2018 of adult first-time kidney-only recipients of paired kidneys from DCD donors, in which one donor resulted in DGF and the other did not. We evaluated outcomes where CIT difference between paired recipients was any, 5, or 10 hours.

Results: Out of 20,059 DCD recipients, 14,545 were excluded for mate kidney non-transplantation, both or neither kidney developed DGF, missing CIT, or mate kidney recipients with equal CIT. The remaining 5,514 paired kidney recipients (2,757 donors) were analyzed. All donor and recipient characteristics were similar except for more non-locally shared kidneys, greater HLA mismatch, and longer pre-transplant dialysis duration in the longer CIT group. On multivariate analysis of DCD kidney recipients, overall graft survival was comparable between recipients with higher CIT relative to paired donor recipients with lower CIT when a CIT difference was present (adjusted hazard ratio [aHR] 1.04, 95% CI 0.91 to 1.19, n=5,514), 5 hours (aHR 1.04, 95% CI 0.85 to 1.27, n=2,710), or 10 hours (aHR 0.88, 95% CI 0.65 to 1.21, n=1,086). Between each of the 3 delta-CIT levels of shorter and longer CIT, there were statistically significant differences in the proportion of delayed graft function at delta any, 5, or 10 hours.

Conclusions: These results suggest that in the setting of DCD kidney transplantation, DGF, specifically induced by prolonged CIT, has limited bearing on long-term outcomes. This may be important evidence that despite the occurrence of warm ischemic injury, kidneys with prolonged CIT offer acceptable outcomes to recipients and are a potential source to expand the donor pool.

Empire Clinical Research Investigator Program (ECRIP) of New York.
316.4

**Evolution and Results of Kidney Transplantation With Donors in Asystole**

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**Introduction:** Before the introduction of the concept of brain death, organs for transplantation were obtained from donors in asystole. Some transplant programs arouse the interest by these types of donors to increase the number of kidney transplants. We analyze the evolution and results of kidney transplants performed in our hospital with asystole donors.

**Patients:** Eighty patients were transplanted with kidneys from donors in asystole, 60 with type II and 20 with Type III Maastricht. This group was compared with recipients of heart beating donors with similar age, sex, number of transplants and HLA matching. Immunosuppression was performed with Prednisone, Tacrolimus and Mycophenolate. The induction was done with ATG-Fresenius or Basiliximab. Acute rejection crises were treated with boluses of Methylprednisolone. ATG-Fresenius was used in corticoresistant rejections.

**Results:** Delayed graft function was more common in asystole donors compared to heart beating donors. Plasma creatinine concentration was significantly better in asystole donors, 1.5 mg/dl versus 1.7 mg/dl. Graft survival was 86% at five years in asystole donor and 88% in heart beating donors. Patient survival was 100% in both groups. Hospitalization of asystole donors recipients was longer and they required more hemodialysis sessions. Acute rejection crises were more frequent in asystole donors recipients.

**Conclusions:** Transplants performed with asystole donors have similar kidney function and survival compared to heart beating donors. Asystole donors can help to increase kidney transplants.

316.5

**Long Term Outcomes of Low Dose Anti-thymocyte Globulin And Anti-interleukin-2 Receptor Antibody Induction in Kidney Transplantation From Expanded Criteria Donors**

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**Background:** Using kidneys from expanded criteria donors (ECD) has been increased due to the shortage of donor organs but seemed to have poorer prognosis. The aim of this study was to evaluate the safety and efficacy of rabbit anti-thymocyte globulin (rATG) induction in kidney transplantation (KT) from ECD compared to anti IL-2 receptor antibody (basiliximab).

**Methods:** We retrospectively analyzed 182 patients who underwent KT from ECDs between April 2004 and December 2020. The patients were categorized into two groups according to induction therapy modality. The basiliximab group (n=43) received basiliximab 20mg/kg on day 0 and 4, while low dose rATG group (n=139) received rATG 1.5mg/kg on day 0, 1, and 2. Both groups received tacrolimus, mycophenolate, and steroids as maintenance immunosuppressive agents.

**Results:** The mean donor age (60.6 vs 64.3, p = 0.007) and KDPI score (84.4 vs 90.0, p = 0.005) were higher in rATG group. Patients in rATG group showed more delayed graft function (11.6% vs 30.9%, p = 0.021) but no significant difference in biopsy proven acute rejection (41.9% vs 35.3%, p =0.546). However, graft survival rates (p = 0.88) and overall survival rates (p = 0.846) were not significantly different between the two groups. CMV infection rate seemed higher in rATG group, but graft survival rate was not influenced by CMV infection (p =0.677).

**Conclusion:** Low dose rATG induction in KT from ECD resulted in comparable patient and graft survival despite the worse donor and recipient profile comparing to basiliximab induction. Therefore, low dose rATG can be considered as an effective and safe induction therapy in KT from ECD.
Comparative Study of Medium Term Outcomes of ABO Incompatible Kidney Transplantation With ABO Compatible Kidney Transplantations

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Introduction: ABO incompatible kidney transplantation has expanded the living donor pool in India where there is lack of an effective deceased donor programme. Though certain studies have shown comparable short term outcomes of ABOiKT vs. ABOcKT, we have evaluated and compared medium term outcomes of the same.

Methods: 75 ABOiKT recipients (ABOiKTR)(case) and 75 age and sex matched ABOcKT (control group) who had undergone kidney transplantation from August 2015 to August 2018 were included in this study. ABOiKTR were desensitized according to institutional protocol. They were followed up on OPD basis and on IPD admissions (if any) from September 2019 till August 2021 for 24 months in the form of clinical evaluations and relevant investigations conducted at interval of 4 months. The outcomes of both the groups were compared in terms of patient survival, graft survival, graft function, incidence of rejections and infective complications.

Results: Most of the patients (54.6%) had IgG Ab titre in the range of 1:128 to 1:512. Highest baseline titre transplanted was 4096. Patients with high titre isoagammaglutinins before transplantation had comparable medium term results with low titre isoagammaglutinin patients. The overall duration (mean ± SD) of follow-up was 57.9 ± 10 months with a median (IQR) of 59.5(50-67) months. The graft function was excellent (S.Cr < 1.5) in 72% ABOc and 73.3% ABOi patients at the end of study period. There was no significant difference in the mean creatinine level at follow up between ABOc and ABOi groups (p>0.05). Patient survival was 93.3% in ABOc and 90.7% in ABOi at the end of study period. There was no significant difference of rejection between two groups. ACR was the most common cause of rejection (4%) followed by ABMR and mixed rejection (2.7% and 1.3% respectively). The highest prevalent serious infection was pneumonia (10.7%) followed by sepsis (7.3%), UTI (6%) and GI infection (6.5%) with no significant association between two groups (p>0.05). No cases of CMV or SKV infection was reported.

Conclusion: The medium term outcome of ABOiKT over 3-6 years was comparable with ABOcKT. Financial cost was also much less in the preconditioning protocol of our institute which included rituximab, plasmapheresis and IVIG. Thus, financially poor patients could afford kidney transplantation from blood group incompatible donors amongst the family members with similar medium term graft outcomes.

ABO – Incompatible Kidney Transplantation in COVID 19 Era: A Single Centre Experience

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Introduction: Though there are multiple studies on outcome of ABO incompatible kidney transplants, we herein present the short term outcome of ABO-incompatible kidney transplantations done in the Covid-19 era.

Methods: We analysed 40 consecutive ABO incompatible kidney transplant recipients undergone transplant from October 2020 till February 2022, followed up till March 2022. Included patients received rituximab 100 mg/200 mg depending on baseline anti ABO titre, plasma exchange and IVIG for desensitization. Target pre transplant anti ABO titre was ≤ 1:64. Patients received induction therapy with anti thymocyte globulin and IV methylprednisolone.

Results: The median duration of follow up was 294 days. The highest baseline titre transplanted was 4096. Patients with high titre isoagammaglutinin patients. The overall duration (mean ± SD) of follow-up was 173 ± 32 months with a median (IQR) of 173(137-205) months. The graft function was excellent (S.Cr < 1.5) in 84% ABOc and 88% ABOi patients at the end of study period. There was no significant difference in the mean creatinine level at follow up between ABOc and ABOi groups (p>0.05). Patient survival was 97.5% each. The single graft and patient loss was due to fungal pyelonephritis. 5 patients (12.5%) experienced episodes of biopsy proven rejection. 3 patients (7.5%) had acute antibody mediated rejection and 2 patients (5%) suffered T Cell Mediated rejection. The post-transplant hospital stay was 12.79 ± 4.61 days. 5 patients needed hospitalisation for infection in the post transplant follow up period. 10 covid-19 recovered patients were transplanted after a mean duration of 88.4 days with mild to moderate severity. 3 patients (7.5%) acquired covid-19 post-transplantation, 2 in early post transplant (<3 months) and 1 patient at 5 months post-transplant period.

Conclusion: There were no significant differences in the patient and graft survival in covid-19 era as compared to our pre covid studies. Rather, they had lower infection rates due to covid-19 related precautions. There was no increase in mortality or infection in a shorter term of follow up of our study period.

Keywords: Short term outcome, ABO incompatible kidney transplantation, Covid19 Era.
316.8

**Successful Desensitization and Transplantation of Kidney Transplant Recipients With Donor Specific Antibodies**

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**Background:** Kidney transplantation has indisputably changed the dynamics of renal medicine and restored hope among patients coming across fatal end-stage renal disease (ESRD). However, sensitization of human leukocyte antigen (HLA) hampers kidney transplantation. Our transplant center used a modified desensitization protocol.

**Methods:** Desensitization protocol in our transplant center encompassed following mentioned strategy to achieve MFI values <1000 and negative CDC crossmatch for both T and B lymphocytes before proceeding for kidney transplantation: Two sessions of Plasmapheresis on day 1 and 2 → Injection Rituximab on day 2 after Plasmapheresis → No Plasmapheresis on day 3 → Eight sessions of Plasmapheresis after day 3 and IVIG 100mg/Kg/ dose after each session of Plasmapheresis → Repeat HLA antibody detection test to confirm if DSAs are present against HLA with MFI values <1000 and CDC crossmatch is negative for both T and B lymphocytes; if NO then continue Plasmapheresis sessions with IVIG 100mg/Kg/dose till MFI values are <1000 and CDC crossmatch is negative for both T and B lymphocytes or if YES then proceed for transplantation → Repeat dose of Rituximab post-transplantation.

**Results:** All the six cases had moderate levels of DSAs against HLA except for one case with MFI value of 17962. With implementation of our modified desensitization protocol, we achieved low levels of DSAs with MFI value <1000 (Table 1). Patients were successfully transplanted with no adverse outcomes, such as kidney allograft rejection, on follow up (Table 2).

**Conclusion:** In our transplant center, we successfully desensitized and transplanted six HLA sensitized kidney transplant candidates with moderate to high DSAs and T and B lymphocyte positive CDC crossmatch. Our desensitization protocol comprised of multiple plasmapheresis sessions with simultaneous low dose IVG and Rituximab. Upon follow up, we did not witness any significant transplant related event such as allograft dysfunction or rejection.

**Keywords:** Kidney Transplantation; Donor Specific Antibodies; Human Leukocyte Antigen; Desensitization Protocol.

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316.9

**Short Term Outcomes of Kidney Transplantation in HLA Sensitized Recipients: A Single-Center Study From Eastern India**

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**Introduction:** Kidney transplantation is acknowledged as a major advance of modern medicine which provides high-quality life years to patients with irreversible kidney failure worldwide. However, ABO and HLA incompatibility remain the two largest barriers to optimal utilization of organs. Sensitization to HLA is the presence of antibody (usually IgG) to HLA in the recipient’s serum which can occur after exposure to antigens as a consequence of sensitizing events like blood transfusion, pregnancy or organ transplant. The present study was aimed to investigate patient and graft survival at one year in HLA sensitized living-donor kidney transplant recipients who underwent desensitization and to determine the incidence of complications including rejection and post-transplant infections.

**Method:** The study was conducted at NH Rabindranath Tagore International Institute of Cardiac Sciences (NH-RTIICS), Kolkata, a tertiary level multispecialty hospital in the city of Kolkata, West Bengal. It was a prospective, observational study. Inclusion criteria were pre-desensitization findings of CDC cross match positivity up to 21% to 40%, Flow Cytometry crossmatch positivity,DSA and/ or SAB positivity. Decreased donor transplants and multiorgan transplant recipients were excluded. A total of 17 HLA sensitized living-donor kidney transplant recipients who underwent desensitization according to institutional protocol were enrolled. Each patient was followed up for one year or till mortality, if earlier.

**Result:** Death censored graft survival was 100%. Patient survival was 76.47%. The mean serum creatinine among survivors at 12 months was 1.21±0.62mg/dl and mean eGFR was 68.86±20.46 mL/min/1.73m². All the survivors had significant change in allograft function among the survivors as measured as biopsy proven early rejection (within one year) was 17.65%. There was no significant change in allograft function among the survivors as measured as eGFR at one year. However, renal transplantation in HLA sensitized recipients is associated with higher rate of infections leading to hospitalization within one year post transplant.

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**Figure 1. Protocol for desensitization of HLA sensitized recipients**

![Protocol for desensitization of HLA sensitized recipients](image-url)
Kidney Paired Donation in Latin America, From Theory To Practice

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Introduction: Between 25-30% of couples will be ABO or HLA incompatible once they finish the transplant protocol. The Kidney Paired Donation (KPD) program is a modality that resolves this incompatibility by allowing donors to be exchanged. Accord to Newsletter transplant 2020, kidney transplant activity in Latin America under the KPD program is null, however there is a Guatemala case report in 2018 where they started this program and another report from 1998 in Mexico with a series of 12 transplant cases renal with exchange of donors. There has been an evolution over time of the KPD at an international level and to date computer algorithms are used based on the blood group of the donor-recipient, sensitization status and the size of the pool of incompatible couples, determining the best probability of matching success within of the program by optimizing the successful matching of donors and recipients according to the principles of fairness, utility and justice.

Method: Observational, analytical, longitudinal and prospective study from December 2018 to July 2021. Were included all G5 KDIGO chronic kidney patients who were HLA or ABO incompatible with their original donors in the pretransplant protocol and who were transplanted under the program of paired kidney donation in the Central Military Hospital, Mexico, City.

Results: 22 kidney transplants were performed under this program. The most common CKD etiology was not determined (ND) with 31.8%. Survival of the graft and the patient 1 year after transplantation was 100%. The post-transplant glomerular filtration rate receptor (GFR) was 72.5 (± 17) ml/min/1.73 m²SC; the GFR post-donación was 75.04 (± 15.98) ml/min/1.73 m²SC. 36.3% of hypersensitized patients were successfully transplanted without plasmapheresis. The mean age of the recipients was 35.67 (± 12.45) years.

The waiting time from admission to the paired program to the transplant was 4.9 months. Inter-hospital donor exchanges have already been carried out; the in-hospital donation rate increased by 33.33%.

Discussion: The Case reports or case series published in latinoamerica’s countries show an adequate evolution of the patients and grafts without major complications as our Hospital.

Conclusion: Transplantation under the paired kidney donation program constitutes a real modality of successful transplantation when there is incompatibility with the original donor. Increased utilization and socialization of this program can increase the country kidney transplantation rate, reducing the waiting list. Our hospital represents the largest published experience in Mexico and latinamerica with this transplant program.

Table 1. Biochemical and histological evolution after kidney transplant under KPD

| Renal | BM, | N | Presence | CR | GFR | ACR | AMR | ABMR | Recurrence | KPDPLICATION | Allograft | Function |
|-------|-----|---|----------|----|-----|-----|-----|------|----------|-------------|-----------|----------|---------|
| 1     | 27.3| 35.3| 0.4       | 40 | 2.3 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 2     | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 3     | 24.7| 0.8   | 0.5       | 45 | 4.1 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 4     | 19.7| 0.3   | 0.6       | 55 | 2.7 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 5     | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 6     | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 7     | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 8     | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 9     | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 10    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 11    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 12    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 13    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 14    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 15    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 16    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 17    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 18    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 19    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 20    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 21    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |
| 22    | 23.5| 0.7   | 0.6       | 55 | 3.4 | FAKMPRON | No | Failing | No | FAKMPRON | No | Failing |

Abstracts

316.11

HLA-DPB1 Molecular Mismatches Are Associated With Acute Rejection and Long-term Graft Function in First Kidney Transplants

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Introduction: It is generally accepted that HLA-DP mismatches (MM) do not impact the survival of first transplants but that they may exert a deleterious effect in retransplants. This study aimed to investigate the impact of HLA-DPB1 allele and molecular MM (mMM) on the occurrence of acute rejection (AR) and low 5-year graft function (5-yGF) in first kidney transplants (KT).

Method: HLA-DPB1 allele and mMM were determined in 130 first KT from deceased donors, performed between 2014 and 2016. The following mMM models were investigated: expression MM, with the high expression G allele in the donor, T cell epitope (TCE) MM, classified as permissive and nonpermissive MM, epitope MM (EMM), considering all six HLA-DPB1 hypervariable regions (EMM-ABCDEF HVR) or only ABEF regions (EMM-ABEF HVR), Eplet MM (EpMM), considering all or only antibody-verified (AbVer) eplets, and solvent accessible amino acid MM (SAMM). EMM, EpMM and SAMM loads were categorized using thresholds determined by ROC analysis for each outcome. The outcomes were AR and 5-yGF (estimated by CKD-EPI).

Results: 119 (91.5%) KT were performed with one or two HLA-DPB1 allele MM. The overall incidence of AR was 17.7% and the median 5-yGF was 40.3 (27.0 - 51.7) mL/min/1.73m2. No association between HLA-DPB1 allele MM and 5-yGF or rejection was observed. Considering only recipients of standard criteria donor, five logistic models for 5-yGF were built including variables that reached a p-value <0.10 in the univariable analysis (age and donor sex, cause of brain death, ABDR MM and AR) and the mMM (TCE, SAMM, all and AbVer EpMM, EMM-ABCDEF and ABEF HVR). In the model 2, variables associated with 5-yGF ≤ 40 were donor age (OR=1.08; CI95%=1.02-1.14; p=0.005) and SAMM≥7 (OR=4.40; CI95%=1.56-12.36, p<0.005), while in the model 4, donor age (OR= 1.09; CI95%=1.03-1.15; p<0.003) and EpMM(AbVer≥2 (OR=3.39; CI95%=1.2-9.45, p=0.02) were associated with low GF. The AUC-ROC for predicting 5-yGF was 0.83 (0.75-0.92) for the model 2, and 0.68 (0.57-0.79) for the model 4. Lastly, for the outcome AR in all recipients, beyond the final donor creatinine, the following mMM models were statistically significant: TCE (HR=3.01; CI95%=1.33-6.84; p=0.008), SAMM≥5 (HR=2.69; CI95%=1.10-6.56; p=0.03), AbVerEpMM ≥3 (HR=3.36; CI95%=1.32-8.70; p=0.01), and EMM-ABCDEF HVR ≥ 6 (HR=2.08; CI95%=2.19-11.82; p<0.001).

Conclusion: To the best of our knowledge, this is the first study that shows that some mMM, in contrast to classical allele HLA-DPB1 MM, are associated with acute rejection and long-term graft function in a population of exclusively first kidney transplants.
Deceased Donor Kidney Transplantation From Donors With Acute Kidney Injury: Realities and Costs

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Introduction: The use of kidneys from deceased donors with acute kidney injury (AKI) is one of the options to expand donor pool. Several studied have reported on the transplantation of kidneys with donor AKI with favorable outcomes. The aim of this study was to investigate the outcomes of kidneys transplantation cases where deceased donors developed AKI before organ procurement.

Material and methods: We retrospectively reviewed the medical records of recipients from January 2016 to November 2021 in a single center. Outcomes in recipients of a kidney graft from a donor with AKI were compared with outcomes in recipients of a kidney graft from a donor without AKI (non-AKI group). Donor and recipient clinical characteristics with creatinine level, delayed graft function rate, length of stay, hospital charge, graft and patient survival rate were investigated.

Results: Total 380 consecutive deceased donor’s kidney transplantation recipients files were studied. The mean follow up time was 40 months. 129 (34%) kidneys were transplanted from AKI donors and 251 (66%) from non-AKI donors. DGF rate was 33% in AKI group and 25.5% in non-AKI group and a trend was mentioned (P= 0.099). 30 days readmission rate was significantly higher among AKI group comparing to non-AKI kidney recipient (45% vs 33.5%, P= 0.02). The mean overall costs of transplantation in AKI group were comparable ($253865 vs $253611 in non-AKI group) (P= 0.97). The mean length of stay (LOS) in AKI group was 6 ± 3.94 days and 6.3 ± 6.3 days for non-AKI group which was almost similar (P= 0.64). DGF rate was increased as AKI stage got higher (18% stage 1, 45% stage 2, 36% stage 3 AKI) (P= 0.03) but no significant difference between AKI stages in terms of LOS (5.53 stage 1, 6.15 stage 2, 6.22 stage 3 AKI P=0.69) and cost ($250290 stage 1, $254892 stage 2 and $255832 stage 3, P=0.91) was mentioned.

Conclusion: Our study shows transplant with donor AKI have comparable outcome in terms of DGF, graft and patient survival rates, hospital charge and length of stay. Although, the 30 days readmission was higher. Our study confirms that grafts from donors with AKI can be used safely and expand donor pool in kidney transplantation without increased cost.

Keywords: kidney transplantation, deceased donor, acute kidney injury, graft.

Table 1.

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<th>Parameter</th>
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<th>non-AKI group</th>
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<td>Donor sex (male/female ratio)</td>
<td>96/33</td>
<td>140/111</td>
<td>0.0003</td>
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<td>Recipient age (mean ± SD, years)</td>
<td>52.09±14.73</td>
<td>48.84±15.47</td>
<td>0.02</td>
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<tr>
<td>Recipient sex (male/female ratio)</td>
<td>81/48</td>
<td>145/106</td>
<td>0.34</td>
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<tr>
<td>PRA (%)</td>
<td>23.31±32.79</td>
<td>26.46±37.34</td>
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<tr>
<td>KPD (%)</td>
<td>47.89±21.17</td>
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</table>

Table 2.

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<th>Stage 3 AKI</th>
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<td>$255832</td>
<td>0.91</td>
</tr>
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<td>LOS (mean, days)</td>
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<td>6.15</td>
<td>6.22</td>
<td>0.69</td>
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<td>DGF rate (%)</td>
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<td>45</td>
<td>36</td>
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<td>30 days readmission rate (%)</td>
<td>36</td>
<td>47</td>
<td>50</td>
<td>0.39</td>
</tr>
</tbody>
</table>

Table 3.

Figure 1.

Legends

Table 1. Donor and Recipients demographics
Table 2. AKI vs non-AKI kidney recipient’s outcome comparison
Table 3. Outcome among different stages of AKI kidney recipients
Figure 1: graft and patient survival rate
316.13

Feasibility and Early Clinical Results of Normothermic Machine Perfusion (NMP) For Kidney Transplantation (NEXT Kidney Trial)

Animeh Singla1, Ramesh De Silva1, Ahmer Hameed1, Taina Lee1, Lawrence Yuen1, Paul Robertson1, Germaine Wong1, Natasha Rogers1, Henry Pleas1.
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Introduction: Normothermic machine perfusion (NMP) is a technique gaining popularity to improve use of marginal deceased organs and reduce ischemic reperfusion injury. This study aimed to determine the feasibility and acceptance of NMP protocol in a single institution.

Methods: From 2017-2020 inclusive, NMP was introduced to the unit in three phases: Pre-clinical, ethics approval with establishment of Kidney assist device (Groningen, Netherlands), establishment of a feasibility study (NEXT Kidney Trial) to establish suitability in routine use. Thus far, we have enrolled a total of 13 patients who received donor kidneys with ex-vivo normothermic machine perfusion between Nov 2020 and February 2022.

Results: The pre-clinical phase involved three years experience using back-bench prepared normothermic machine perfusion adapted from existing cardiopulmonary bypass pump device. Initially it utilised porcine, and later discarded human kidneys to establish protocol and fluid constituent to be utilised. Clinical introduction had two components: device training and device learning curve (n=2 cases). Transplant coordinators and perfusionists experienced with pre-clinical and clinical component of the device introduction were critical to the feasibility study. 13 deceased donor kidney transplants occurred using donors after circulatory determinant of death (DCD). The mean age was 44.8 years old, with average warm donor ischemia time of 17.1 minutes. The median kidney donor profile index (KDPI) was 66. Of these, 8 (62%) had primary function and 5 (38%) experienced delayed graft function (DGF) and required dialysis within 7 days post transplants. Of patients with DGF, the median number of dialysis sessions was x1. The average NMP flow at 54 minutes into the perfusion which subsequently developed DGF. The mean recipient age was 44.8 years old. Mean cold ischemia time (CIT) and secondary warm ischemia time (SWIT) were 485 min (SD 127min) and 19.8 min (SD 2.7min) respectively. Incidence of delayed graft function was 38% (n=5), presented in table 1. Mean CIT for DGF and IGF was 494 min and 470 min. The mean terminal donor creatinine for DGF and IGF cohorts were 135micromol/L and 97 micromol/L.

Conclusion: Utilisation of NMP protocol into an established kidney transplantation unit is feasible based on early clinical results. A multidisciplinary approach involving experienced perfusionists, transplant coordinators and physicians is critical to the success of the program.

316.14

Impact of Donor Hepatic Steatosis on Kidney Transplant Recipient Outcomes

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Introduction: Increasing evidence suggests an independent association of hepatic steatosis with chronic kidney disease, kidney function decline and risk of cardiovascular (CV) disease. Whether the presence or severity of an organ donor’s hepatic steatosis impacts on kidney transplant recipient (KTR) outcomes has not been studied.

Methods: We performed a retrospective cohort study of deceased liver donors, matched to their KTR, in New South Wales (NSW), Australia from 2006-2020. We linked data from the Australian and New Zealand Dialysis and Transplantation (ANZDATA) and Organ Donation (ANZOD) registries with biopsy results of donor livers evaluated or utilised for transplantation at the NSW state-wide liver transplant unit. Donor hepatic steatosis was graded contemporaneously by histopathologists as S0 (<5%), S1 (5-33%), S2 (>33-66%) or S3 (>66%). Standard donor and recipient characteristics were collected. All-cause death, cardiovascular (CV) death, graft loss (deceased-donor or delayed graft function (DGF), graft function decline (assessed by eGFR) and post-transplant CV events (composite of coronary artery, peripheral vascular or cerebrovascular disease) were compared among recipients according to their presence and severity of hepatic steatosis.

Results: 751 donors with liver biopsies were matched to 1,263 KTRs (8,043 person-years follow-up). Donor hepatic steatosis grades were: S0 453 (60%), S1 195 (26%), S2 71 (9%), S3 32 (4%). Donors with hepatic steatosis (S1-3) were significantly older (median age 53 vs 46 years) than those without steatosis and had worse metabolic profiles: higher body mass index (median 27 vs 25kg/m2), diabetes (9% vs 6%), hypertension (35% vs 25%), KTR of donors with and without hepatic steatosis had similar baseline characteristics. Presence of hepatic steatosis (vs no steatosis) and steatosis severity (S3 vs S0-2) did not impact on all-cause- or CV-death, graft loss, or DGF in the multivariable analysis. Univariable analysis suggested that decline in graft function was greater in recipients from donors with steatosis compared to recipients of donors without steatosis, but this no longer remained significant on multivariable analysis after adjusting for other variables. There was an increased risk of CV events on univariable (HR 1.42, 95%CI 1.00-2.02, p=0.05) and multivariable analysis (HR 1.47, 95%CI 1.03-2.10, p=0.04, Table 1) among recipients of donors with severe (S3) steatosis versus those with no/less donor steatosis.

Conclusion: In this retrospective analysis, neither the presence nor severity of biopsy-proven donor hepatic steatosis appeared to impact kidney transplant recipient outcomes. Recipients from donors with severe hepatic steatosis may be at higher risk of cardiovascular events.

Table One: Multivariable cox-proportional hazards survival analysis for time to first cardiovascular events in kidney transplant recipients

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age (per year)</td>
<td>1.03 (1.02-1.04)</td>
</tr>
<tr>
<td>Recipient female</td>
<td>0.70 (0.58-0.85)</td>
</tr>
<tr>
<td>Recipient diabetes</td>
<td>1.82 (1.38-2.40)</td>
</tr>
<tr>
<td>Recipient kidney disease cause</td>
<td>&gt;0.001</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>1</td>
</tr>
<tr>
<td>Diabetic kidney disease</td>
<td>2.11 (1.52-2.95)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.86 (1.37-2.54)</td>
</tr>
<tr>
<td>Other</td>
<td>0.98 (0.79-1.22)</td>
</tr>
<tr>
<td>Donor severe (S3) hepatic steatosis</td>
<td>1.47 (1.03-2.10)</td>
</tr>
<tr>
<td>HLA mismatch (per each)</td>
<td>1.09 (1.05-1.14)</td>
</tr>
<tr>
<td>Transplant year (per year)</td>
<td>0.96 (0.93-0.98)</td>
</tr>
</tbody>
</table>

CI = confidence interval; HLA = human leukocyte antigen; HR = hazard ratio
Kidney Transplantation in Highly Sensitized Patients: A Single Center Results

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Introduction: Kidney transplantation in highly sensitized patients (HSP) is recognized as a complex problem all over the world. More than 20% of potential kidney transplant recipients have pre-existing anti-HLA antibodies. These patients remain on the waiting list longer, and their long-term outcomes are usually worse due to the high risk of antibody-mediated rejection. This determines the need for a special organ allocation approach, as well as desensitization protocols. The aim of this study was to evaluate antibody-mediated rejection rate, 5-year patient survival rates and incidence of complications after kidney transplantation in HSP and non-sensitized patients.

Materials and Methods: The study included 198 patients who underwent kidney transplantation from deceased donor between January 2015 and December 2017. 48 patients with PRA> 40%, or anti-HLA antibodies> 6000 MFI were defined as HSP. The control group included 150 non-sensitized patients. All HSP underwent desensitization before kidney transplantation. Desensitization protocol for HSP included one of the extracorporeal methods of immune complexes removal (therapeutic plasma exchange with replacement of up to 2 volumes of circulating plasma volumes or semiselective immunoadsorption with a regenerating column), as well as intravenous administration of pharmacological agents depressing the synthesis of antibodies (2 g/kg of intravenous immunoglobulins and 375 mg/m² of anti-CD20 antibodies (rituximab)). Kidney transplantation was performed if negative result of cross-match. All HSP received methylprednisolone 10 mg/kg just before reperfusion and 10 mg/kg antithymocyte antibodies for 7 days after transplantation as induction therapy. Maintenance immunosuppression included tacrolimus, mycophenolic acid, and methylprednisolone. HSP were also separated in a high-priority group if negative cross-match appearing during organ allocation.

Results: HSP had higher antibody-mediated rejection rates compared to control group (25% vs. 6.1%, p<0.01), and lower 5-year cumulative graft survival compared to control group – (71% vs 93%, p<0.01) (Figure 1). The difference in 5-year patient survival rates between HSP and control group was not statistically significant (89% vs 97%, p=0.12). The difference in 5-year patient survival rates between HSP that were transplanted and HSP on the waiting list 5-year patient survival rate (89% vs 60%, p=0.07) (Figure 2). There were 46 cases of complications in kidney transplant recipients during the observation period. The incidence and structure of postoperative complications did not differ significantly between HSP and non-sensitized patients.

Conclusions: Despite higher occurrence of antibody-mediated rejection in HSP group, the 5-year patient survival rate after kidney transplantation in this group is remarkably higher than in HSP on waiting list.
Which Patients Over 60 Years Old Are Candidates for a Kidney Transplant? Usefulness of a Mortality Predictive Score

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Introduction: The decision to indicate a kidney transplant (KT) to an elderly patient with end-stage chronic kidney disease is not simple due to the high morbidity and mortality associated. The Dusseux et al. score was originally developed in France to predict 3-year post kidney transplant mortality in subjects older than 70 years. The objective of this study was to evaluate the usefulness of this score to predict 1-year post KT mortality in patients older than 60 years and to identify the best cut-off point.

Methods: A retrospective cohort study was performed. All patients over 60 years old who received a KT at Hospital Privado Universitario de Córdoba between January 2009 and December 2015 were consecutively included. A one-year post-KT follow-up was carried out and variables associated with mortality were analyzed. The Dusseux et al. score considers as predictive variables: sex, age, etiology of chronic kidney disease, comorbidities, mobility status, body mass index and the presence of a temporary catheter at the time of dialysis initiation. The t test or Mann-Whitney test were used to evaluate differences between continuous variables t, and chi2 or Fisher’s test for categorical variables, as appropriate. To evaluate the predictive capacity, the area under the curve (AUC) was used and the Youdex Index J was applied to identify the best cut-off point, with its sensitivity and specificity. Kaplan Meier survival curves were made and then compared with the logRank test. A value of p<0.05 was considered statistically significant.

Results: We included 111 patients aged 66.2 ± 5.2 years, 54.9% were men. As relevant comorbidities, 30.7% were diabetic and 13.5% had ischemic heart disease. 82% received a cadaveric KT. As induction, 100% were given steroids, 60.3% basiliximab, 22.5% thymoglobulin and 9.9% gamma globulin. As maintenance, 93.7% were treated with steroids, tacrolimus and mycophenolate. Mortality during follow-up was 9.9% (n:11; 8 due to infectious etiology and 3 from cardiovascular disease). The patients who died were older (70.3 ± 6.6 vs 65.8 ± 4.9; p=0.05), had a greater history of ischemic heart disease (36.7% vs 11%; p=0.04), and had a higher mortality predictive score (9.4 ± 3 vs 6.8 ± 2.5, p=0.02). There were no differences in the rest of the variables. This score obtained a high AUC to predict mortality (AUC=0.75; p<0.01; figure 1) and the best cut-off point was 8, with a sensitivity of 72.7% and a specificity of 78%. Subjects with a score >8 had higher mortality than those with a score ≤8 (26.7% vs 3.7% respectively; p<0.01). There were significant differences between the survival curves of these groups (p<0.01; figure 2).

Conclusion: This clinical score is a good predictor of mortality 1-year after KT in patients over 60 years old. The best cut-off point of the score was 8 points. This could be a useful and simple tool to help in the decision to indicate a KT in this type of patients.

Fundación Nefrológica de Córdoba.
Do All the Expanded Criteria Donors Offer the Same Outcome? A Comparison From a Single Center

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Introduction: The quality of deceased donors is gradually worsening and the clinical category of expanded criteria donor (ECD) includes an always increasing donor population, but not all the single kidney transplants (SKTx) from ECD seem to have similar results. We analyze the outcome of SKTx from ECD stratified by age and compared to SKTx from standard criteria donors (SCD).

Method: We considered patients underwent SKTx to our Center from January 2005 to December 2021. We considered 4 groups: Young (Y)-ECD, SKTx from ECD 50–59-year-old with at least 2 features between: creatinine >1.5mg/dl, arterial hypertension or cerebrovascular accident, in any combination; Aged (A)-ECD: SKTx from ECD 60–69-year-old; Elderly (E) ECD: SKTx from ECD ≥70 year-old, and the Control (C)-SCD: SKTx from SCD <60 year-old. Groups were compared for primary non function (PNF), delayed graft function (DGF), vascular thrombosis, urinary leakage, acute rejection rate, cumulative complication index (CCI), e-GFR (CKG EPI), 1-, 5-, 10-year patient survival.

Results: Overall 354 patients underwent SKTx: mean donors age was 53.6 ±17.1 years, mean BMI was 25.4 ±3.9. C-SCD-n=181 and 173 (48.9%) were from ECD, stratified as follows: Y-ECD-n=31, A-ECD-n=62, E-ECD-n=80. The main characteristics of the donors and recipients in the study population are reported in the Table 1 and 2. The groups presented differences in donors age (p<0.0001), median KDPI (<0.0001), median Remuzzi-Karpinsky biopsy score (p= 0.002) and rate of cerebrovascular events as cause of donors death (p<0.0001). The main results of the analysis are reported in the Table 3. Regarding the outcomes, there were no differences in terms of PNF, DGF, CCI, acute rejection and vascular thrombosis rates. The urinary leakage occurred more frequently in E-ECD (p=0.04). The 3-month e-GFR have been superior in C-SCD than the other three groups (p=0.01 vs Y-ECD; p<0.0001 vs A-ECD; p<0.0001 vs. E-ECD). Same advantage in favor of C-SCD was recorded for 1-year and 5-years eGFR (p<0.0001 and p=0.019).

Conclusion: The SKTx from ECD present a significantly lower e-GFR compared to the others ECD and to C-SCD. Nevertheless, all SKTx from any ECD have post-operative outcome similar to C-SCD and comparable patient and graft survival, in short and long-term. E-ECD, when used for SKTx, should be used in carefully selected recipients with limited needs in terms of deputation (elder, small in size, little musculature). Moreover, a larger use of calcineurin inhibitor free immunosuppressive regimens could improve results in long term.
**317.1 Personalized Approach to Risk-Stratified Desensitization in Modified Multivisceral Transplantation**

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**Introduction:** Human leukocyte antigen (HLA) allosensitization prolongs waitlist times and can increase the risk of rejection and both graft and patient loss for intestinal transplant candidates. Desensitization offers a potential therapeutic option to facilitate transplantation with a more compatible donor however there is paucity of evidence on the field. We aim to describe a personalized approach to risk-stratified desensitization in a modified non-liver multivisceral transplant (MVT) candidate with cPRA of 100%.

**Method:** A 45 y.o female with history of multiple severe gastroparesis and pseudoobstruction on chronic parenteral nutrition, sensitized via multiple blood transfusions and pregnancy x 2 actively listed for modified MVT was prospectively followed up to determine risk stratification desensitization based on HLA and C1q antibodies (Ab) tests. She underwent desensitization with Rituximab 375mg/m2 x 1, therapeutic plasma exchange (TPE) x 5 sessions in March 2021 followed by 2g/k monthly IVIG x 6. We report her follow up at 12 months since the therapy.

**Results:** Before starting desensitization strategies, she tested positive for T and B cell virtual cross match (VCM) with all her donor offers. Her cPRA was 100 % with 54% for Class I (dominant HLA Ab: B7: 22775 MFI) and 63 % of class II (dominant HLA Ab: DR17: 21021 MFI). Following desensitization strategy, we identify using C1q test her dominant HLA Ab as B7, B81 and DR4 with 17321, 8619 and 3133 MFI's respectively; therefore, they were classified as unacceptable antigens. A donor’s offer was accepted when her HLA ab were deemed appropriate in the context of T cell VXM negative and the expected B cell VXM positive (6.48 ratio) by flow cytometry. She underwent modified MVT in August 2021. The patient received induction immuno-suppression with Methylprednisolone taper, Rituximab 150 mg/m2, anti-thymocyte globulin 2 mg/kg x 5 doses, TPE x 3 sessions, Vedolizumab 300 mg IV 10, 30 and 60 days post transplant. Her current maintenance immunosuppression is with tacrolimus (target trough level: 8-10ng/ml now 7 months post transplant), mofetil mycophenolate 500 mg twice daily and prednisone taper to 5mg daily. Her dominant donor specific antibody (DSA) was DR7, which decreased on pre-transplant sample from 13982 to 3053 MFI post induction treatment a week after finishing TPE. The patient’s protocol biopsies showed no evidence of rejection. At 7 months post transplant her DR7 DSA remains low at 1576 MFI and there is no evidence of de novo DSA.

**Conclusion:** We described the use of personalized approach to risk-stratified desensitization that lead to accept an organ offer based on HLA and C1q antibodies test follow by tailored immunosuppression strategies with early successful results. Further studies are needed to reproduce our outcomes.

**317.2 Immune Profiling of Migrating and Graft-Associated γδ T Cells After Human Intestinal Transplantation Reveals Unique Innate and Adaptive Features**

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**Introduction:** Innate- and adaptive-like features of human γδ T cells are associated with different T cell receptor (TCR) repertoires, defined as γδVδ1+ and non-γδVδ2+, respectively. Immune repertoires can be shaped by tissue compartmentalization, age and history of antigen exposure. Despite comprising a significant portion of lymphocytes residing in many organs, including gut, the role of γδ T cells in transplantation outcomes is unclear.

**Methods:** Serial biopsies from intestinal transplantation (ITx) recipients allow us to investigate the turnover dynamics of intragraft γδ T cells in the presence and absence of rejection, providing a unique opportunity to study the fundamental biology of human γδ T cells. Clonal tracking of γδ T cells in intestinal grafts, peripheral blood and bone marrow (BM) at both pre- and post-Tx time points provides a deeper understanding of their tissue origin, migration pattern and phenotypic maturation. Integrated Repertoire (γδ T cell primer sets) and 10x Genomics (5’cDNA library) platforms were applied to relate functional gene profiles within individual γδ T cell clonotypes.

**Results:** We previously demonstrated that donor γδ T cell macrochimerism (peak level ≥4% in blood) is associated with less rejection. We now show that high levels (>10%) of γδ T cell blood chimerism were only observed in patients with macrochimerism. Remarkably, donor γδ T cells were detected in recipient BM 105–357 days post-Tx. Single-cell profiling of BM-infiltrating donor γδ T cells revealed both Vδ1- and Vδ2-dominant clonotypes with cytotoxic effector phenotypes that might contribute to graft-vs-host responses. In one multisurgical Tx patient, the top dominant donor γδ TCR clone (VγδVδ1) detectable during the peak T cell chimerism in blood (8–20 days post-Tx) was also predominantly present in the recipient BM 126 days post-Tx, with clear cytotoxic profiles (GZMB/PRF1/GLY) but reduced proliferation (MK67) and BM-homing (CXCR4) features. BM-infiltrating donor Vδ2 clonotypes tended to be more “public” and were shared by three pediatric patient post-Tx BM specimens and pre-Tx repertoires across pediatric donors and tissues. Many of these Vδ2 clones are Vγδ9 with zero N-adDITIONs that likely originate from fetal liver and cord blood. However, these Vδ2-dominant clones were not present in adult lymphoid tissues, gut or BM, suggesting an age-related distribution and migration pattern. In contrast to γδ T cells, the turnover dynamics of γδ T cells in the graft showed a stronger association with donor age than with the status of macrochimerism. Graft-repopulating recipient γδ T cells showed activated effector phenotypes early post-Tx and gradually developed into cytotoxic resident-memory T cells with “private” Vδ1 clonotypes.

**Conclusion:** γδ T cells have the potential to modulate immune responses to influence T cell chimerism locally and systemically. They may participate in host defense and graft rejection after ITx.
317.3

**Association of CD4+CD25highFoxP3+ Regulatory T-Cell Frequency With Graft Outcome Upon FK506 Treatment in an Experimental Small Bowel Transplantation Model**

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**Background:** Intestinal transplantation (ITx) is the only curative option in patients with irreversible intestinal failure showing complications in parenteral nutrition. However, the immunological load of the gut makes the rejection rate to be higher than the rest of solid organ transplants (80% within the first 90 days after surgery), the graft loss rate and need for re-transplantation at 1, 5, and 10 years 29%, 50%, and 59%, respectively, and the 10-year survival of only 43%. Therefore, new strategies aiming to down modulate host vs. graft response are crucial to improve ITx long term results. Regulatory T-cells (Tregs) are key players in the induction/maintenance of peripheral tolerance, nonetheless their relevance in ITx in almost unexplored. We study the Treg migration/expansion kinetic and its association with the allograft outcome in an experimental ITx model.

**Methods:** We used a rat heterotopic and allogenic ITx model in which Brown Norway small bowel (jejunum and ileum) was engrafted into Lewis animals. We used as a first line treatment not only controlled the allogeneic response better than Rapamycin (no significant clinical or histological changes were observed at day 14 after surgery), but also enabled a more gradual exchange of donor/recipient lamina propria T-cell compartment and the expansion of both blood and graft Tregs (p<0.01). Interestingly, animals that received FK506 during 1 week and then remained 7 days without immunosuppression, a period proven sufficient for developing an allogeneic response and subsequent tissue damage, still preserved increased Tregs frequency and remained free of ACR. Of note, in these group none of the analyzed genes showed increased mRNA expression at day 14 post-transplant.

**Results:** Rapamycin and non-treated animals showed significant clinical and histological deterioration since day 7 post-transplant (mild-moderate ACR at day 7 and severe ACR at the days 10-12, p<0.05). The allogeneic response was associated with loss of T-cell chimerism (p<0.05), diminished graft Treg frequency (p<0.01) and increased mRNA expression of MCP-1, IL-6, TNF, IFNγ, CCL11, CXCL10, IDO, and TGFB (p<0.05). On the other hand, FK506 used as a first line treatment not only controlled the allogeneic response better than Rapamycin (no significant clinical or histological changes were observed at day 14 after surgery), but also enabled a more gradual exchange of donor/recipient lamina propria T-cell compartment and the expansion of both blood and graft Tregs (p<0.01).

**Conclusion:** In our animal model increased Treg frequency was associated with graft protection even when immunosuppression was withdrawn. Thus, strategies promoting their expansion would be desirable to improve long-term outcomes.

Authors want to thank NUPA foundation (Spanish Association of Help to children with Intestinal Failure, Parenteral Nutrition and Multivisceral Transplant) for their support.

317.4

**Bilateral Hand Transplantation at a Tertiary Care Centre in India**

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**Objective:** To assess the outcomes of 11 hand transplant patients who underwent transplant at Amrita institute of medical sciences, Kochi, India.

**Materials and methods:** This is a retrospective, cross sectional observational analysis of 11 hand transplant patients who underwent hand transplant at Amrita institute of medical sciences, Kochi, India.

**Results:** 11 patients underwent hand transplant from 2015 to 2022. All patients received bilateral hand transplant. Average age at transplant was 31years (24yrs to 52 yrs). The mean follow-up of these patients were 2yrs. The cause of hand loss was due to electrical burns (n=5); crush injury (n=4) and blast(n=2). All patients were induced with ATG and maintenance immunosuppression was tacrolimus, mycophenolate mofetil and prednisolone. The average cold ischaemia time was 320 minutes for each limb and the average warm ischaemia time was 15 minutes. 7 out of the 11 patients had at least one episode of rejection (all were acute cellular rejection). The average number of rejection was 2.5 episodes. Rejection occurred within the first two months. Most rejections were successfully treated with steroids. One patient alone received IVIG and rituximab for rejection but never occurred again. The infectious complications noted were CMV colitis (n=1), herpes labialis (n=1), Giardiasis (n=1). One patient developed monomorphic B cell lymphoma of the gastrointestinal tract which was successfully treated with Rituximab and cure was attained. One of them had graft loss and amputated one limb and one patient expired due to complications of sepsis. Rest all were functional.

**Conclusions:** Hand transplant’s long term functional status remains good. With advances in immunosuppression and treatment for the complications this can be offered to a wider population.
Novel Biologic Therapies to Promote Functional Recovery in Limb Transplantation

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Introduction: Vascular composite allotransplantation (VCA) such as limb and face require successful nerve regeneration and reinnervation of graft for optimal functional outcome. We investigated whether biologic therapies such as mesenchymal stem cells (MSCs), Granulocyte-Colony Stimulating Factor (G-CSF), and/or Dihexa (novel neurotrophic peptide) can improve sensory and motor functional recovery in rat sciatic nerve transection repair and limb transplant models.

Materials and Methods: in sciatic nerve transection repair model, under general anesthesia, individual branches of right sciatic nerve (tibial, peroneal and sural) were identified and transected. After an hour the epineurium of the proximal and distal ends of respective nerves were approximated using 10-0 sutures. In limb transplant model, the donor rat hind limb was harvested at the mid-femoral region transecting sciatic nerve and stored on ice (< 2 hours) until recipient rat was ready for orthotopic syngeneic transplantation. The nerve ends were approximated and vessels were anastomosed using vascular cuff technique. Autologous bone marrow derived MSCs (5x10⁶; passage ≤6), G-CSF (50 µg/kg), (Dihexa 2 mg/kg) or Vehicle were administered topically at the nerve repair sites and i.v./i.p. The motor function was assessed by walking track analysis and sensory function by cutaneous reaction test at 1-2 week intervals post-surgery.

Results: At two weeks post-nerve repair, total sensory nerve function in all groups was ~1.5 on a scale of Grade 0-3 (0=No function; 3=Normal function); however, peroneal nerve function ranged 2.6-3.0. By 4 weeks total sensory function was 2.2±1.0, 2.0±1.2, 2.2±1.1 and 1.8±1.3 in MSC, G-CSF, Dihexa and Vehicle groups, respectively (Figure 1; Dihexa not shown was similar to MSC). At 10 weeks, normal sensory function (~3) was restored in all groups (n=8/group). Improved sensory function with biologic therapy suggested increased nerve regeneration. The sciatic function index (SFI) a measure of motor function (0=normal function; -100=nonfunctional) during 5-16 weeks was markedly improved in G-CSF group (-40 to -26) compared to MSC (-93 to -66), Dihexa (-85 to -57) or Vehicle (-110 to -45) group (Figure 1). The novel biologics improved motor function. However, ~30% atrophy of gastrocnemius muscle in all groups was probably due to limb disuse and suboptimal re-innervation. In limb transplants, sensory function recovery was slow and ranged 0.8 to 1.3 by 8 weeks, and 1.5 to 2.0 by 16 weeks post-surgery. Majority of the transplants (~60%) developed flexion-contractures and we were unable to calculate SFI in all animals. However, fewer animals in G-CSF (3 out of 8) group compared to Vehicle (4 out of 6) developed contractures. SFI values were marginally better in G-CSF group. Ex vivo expanded MSCs demonstrated characteristic markers: CD29+, CD90+, MHC Class I+, CD34-, CD31-, Class II+, and were pluripotent.

Conclusions: MSC, G-CSF and/or Dihexa therapies appear promising to promote sensory and motor function recovery in VCA.
Anti-donor Human Leukocyte Antigen (HLA) Antibody Response After Vascularized Composite Allotransplantation: A Multicenter Study

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Introduction: The clinical significance of donor-specific anti-HLA antibodies (DSAs) in vascularized composite allotransplantation is not clear, even though their occurrence has been reported by several teams. The aim of the present multicenter study was to assess the incidence of DSAs in upper extremity (UET) and face transplanted patients and their influence on patient outcomes.

Methods and Results: Pre- and post-transplantation sera of 37 patients (23 UET, 13 face transplantsations and 1 simultaneous UET and face transplantation) were screened in a single laboratory using a solid phase assay. The recipients included 29 men and 8 women, median age was 33 years. Their immunosuppressive treatment, number of HLA mismatches, number of acute rejection (AR) episodes with Banff score, occurrence of graft vasculopathy, chronic rejection and graft loss were collected. In addition, the histological impact of DSA was studied in a small cohort of these patients. For each patient from our cohort with de novo DSA, we randomly selected 2 biopsies taken before and 3 biopsies after the appearance of DSA. DSA were detected in 43.2% of the recipients (16/37), including 6 patients who had presented preformed DSA. The intensity of recipient humoral alloimmune response was estimated using the MFI of positive beads in solid-phase assays. This showed variability both among recipients and among the different DSA specificities of the same patient. From an overall perspective, the alloimmune response was not very strong (median MFI 1413). Donor and recipient age and gender as well as the immunosuppressive treatment were not statistically different between the recipients who developed DSA and those who did not do it. Interesting the number of AR and Banff score did not influence DSA occurrence. No significant correlation between the presence of DSA and chronic rejection, graft vasculopathy or graft loss was found. Five patients with DSA developed chronic rejection and 4 of them graft vasculopathy. In addition, 2 recipients with DSA experienced several episodes of atypical rejections. Longitudinal assessment showed that almost all preformed DSA disappear over time and almost 50% of de novo DSA also in those patients who developed chronic rejection and/or graft vasculopathy with graft loss. There were 5 cases of graft loss and 3 of which had developed DSA during their follow-up. The histopathological study performed on skin sections obtained after the appearance of DSA (routinely-stained and immunolabelled for CD34) did not show significant influx of inflammatory cells into the dermal capillaries endothelial, cell swelling, or microthrombosis.

Conclusion: The study confirms that VCA is a sensitizing event for recipients. However, the evolution of DSA over time seems rather heterogeneous. Pre-formed DSAs tend to disappear rapidly and potentially no longer be detected, contrary to de novo DSA whose evolution and pathogenicity remain to be elucidated. Longer follow-up will allow to better assess the outcomes of the patients who developed DSA.

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qPCR Based Immunotherapy in Intestinal Transplant Recipients and Candidates

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Introduction: Inflammatory bowel disease (IBD) in intestinal transplantation (ITx) recipients and candidates is a complication that may be the result of an immune dysregulation due to the immunosuppression or the underlying disease. Conventional treatment of IBD, including corticosteroids and immunotherapy with monoclonal antibodies, uses to be effective, but in some patients the inflammation is refractory to the treatment. The aim of the study was to determine the intestinal mucosa cytokine expression in order to establish the optimal therapy in two multivisceral recipients and two ITx candidates with persistent enteritis.

Methods: Two multivisceral recipients with episodes of ulcerative enteritis refractory to corticosteroids and infliximab treatment were studied, as well as, two ITx candidates with intestinal failure and inflammatory colitis and enteropathy, respectively. Mucosal biopsies were taken from affected and healthy areas and frozen in RNAlater until RNA extraction. Expression of cytokine genes which are targeted by approved drugs (IL1B, IL6, IL12p70, IL17A, IL23 and TNF) was determined by qPCR. Gene expression was calculated as 2-ΔΔCt using GAPDH as endogenous control.

Results: ITx recipients (Patients 1 and 2); both patients (13 and 14 years old males) developed in the late posttransplant ulcerative ileitis and ulcerative colitis respectively. They were initially treated with metiprednisolone without achieving endoscopic improvement. Graft cytokine expression in pre-treatment biopsies of healthy and inflamed area was carried out, both of them showing a significant increase of IL6, correlating with high IL6 plasmatic levels (Figure 1A and 1B). Tocilizumab was then administered every two weeks, getting the clinical resolution in two months. ITx candidates: Patient 3 was a 5 years old male with trichohepatoenteric syndrome, showing ulcerative colitis. He was treated with corticosteroids without endoscopic or clinical improvement. Intestine cytokine expression in pre-treatment biopsies was carried out objectifying elevated IL1 and IL6 levels, so he was treated with Tocilizumab achieving great healing of the colitis (Figure 1C). Patient 4 was a 1 year old male suffering from autoimmune inflammatory disorder with a mutation in mevalonate kinase gene, having enteropathy. He was empirically treated with Infliximab with initial improvement, but having a deterioration afterwards. Intestinal cytokine expression in pre-treatment biopsies showed elevated IL1, IL6 and TNF levels (Figure 1D). He was treated with Anakinra without clinical improvement, changing for Adalimumab achieving clinical resolution.

Conclusions: In the context of mucosal inflammation, the analysis of intra-graft cytokine expression by qPCR is a useful and affordable tool to guide the treatment in a personalized way, showing a high effectiveness of the therapy.

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Introduction: Donor specific anti-HLA antibodies (DSA) impact negatively on the outcome of intestinal grafts. Although the use of antibody-removal therapies (ART) is becoming more frequent in the last years, issues regarding their timing and effectiveness remain under discussion, especially when they are detected in the absence of any clinical symptom.

Methods: From an initial cohort of 119 transplants, 81 transplants were finally included in the analysis (those without anti-HLA study or in which donor specificity could not be assessed were discarded). ART was performed with different combinations of intravenous immunoglobulin (0,5 g/kg), plasmapheresis and rituximab (boluses of 375 mg/m² with a maximum of 4 doses). Anti-HLA antibodies were tested by Luminex assay.

Results: A total of 14 ART procedures were performed in 12 transplants from 10 recipients (Table 1) under the following indications: A) peri-transplant due to preformed DSA (n=3), B) DSA in the context of rejection (n=4), C) dnDSA without rejection (n=5) and D) DSA persistence (n=2).

Considering as successful outcomes both the complete DSA removal and the partial decrease (in number of specificities and/or DSA intensity), ART resulted effective in the 79% of the procedures (11/14), 83% of transplants (10/12) and 90% of recipients (9/10). Regarding the indication, ART showed a 100% effectiveness in patients treated for dnDSA without clinical symptoms, whereas it decreased to 67% for preformed DSA and DSA in the context of rejection (needing in some cases more than one procedure to achieve the complete clearance). Analyzing the impact of DSA MFI on the ART outcome, we observed that it was significantly higher in persistent than in cleared DSA (p=0.016) (Figure 1A). This difference was mainly attributed to DSA-II, in which MFI values showed to be much more decisive for DSA removal (p=0.012).

Another factor relevant for the therapy success was the time between DSA detection and ART starting, this being significantly lower for cleared DSA (p=0.003) (Figure 1B). The 8-year allograft survival in treated recipients was similar to those without DSA. Nevertheless, non-treated patients with DSA showed a significantly lower graft survival (p=0.003) (Figure 1C).

In the 3 transplants in which dnDSA appeared together with rejection the graft loss was unavoidable even if the ART was effective in 2 of them. From the remaining 9 cases, 7 transplants were free of rejection. In another 2 cases rejection happened without compromising graft viability and without DSA increase.

Conclusion: The results confirm the ART effectiveness in terms of DSA removal and allograft survival and encourage their early use even in the absence of clinical symptoms.
Report of a Case of Double Arm Transplantation Including Left Shoulder Reconstruction

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Introduction: Although arm transplantation was proposed as a therapeutic option in arm amputees, only 14 cases were reported.

Objectives: A double arm transplantation including reconstruction of the left shoulder was performed on January 13, 2021 in Lyon (France). We report the results one year after the transplantation.

Materials and Methods: The recipient was a 48-years old patient with bilateral amputation at proximal arm level after electric shock in January 1998, who underwent liver transplantation in 2002. He received the grafts from a deceased 35-year old male donor. In the recipient on the right side donor humerus was fixed on the remaining 9 cm-long proximal stump, which was reinforced with the donor fibula in an intra-medullary fashion. On the left side the whole donor humerus including the humeral head was transplanted, with reconstruction of the gleno-humeral joint capsule by performing a suspension ligamentoplasty. On the right side the anastomoses were performed between donor and recipient axillary arteries and veins; on the left side the arterial anastomoses were performed between donor and recipient subclavian arteries and the venous anastomosis between donor subclavian vein and recipient jugular vein; Nervous repair was at the proximal nerve level on the right side and at level of the brachial plexus trunks on the left side. Both deltoid muscles were transplanted: on the right side it was used to assure skin vascularization; on the left side the recipient deltoid muscle was reinserted and the donor one was reported posteriorly with its innervation. Cold ischemia time was 101 minutes on the right side and 133 minutes on the left side. Continuous hemodialysis was performed during the surgical procedure to reduce reperfusion-induced ischemic disorders after revascularization. The immunosuppressive protocol included antithymocyte globulins and tacrolimus, steroids and mycophenolate mofetil. An intensive rehabilitation program was initiated since the first post-operative day.

Results: In the first post-operative period partial thrombosis of the venous bypass occurred and an anticoagulant treatment was started with consequent hematoma in the left pectoralis, which was successfully treated with percutaneous drainage. A specific antibiotic therapy was given against Propionibacterium acnes, evidenced in the biopsies performed on the recipient’s bones during the transplantation.

Twenty days after transplantation the patient developed a Banff grade 2 acute rejection episode on both arms, which disappeared after IV steroids and clofibasil and tacrolimus creams. The patient suffered neuropathic pain at level of the grafted upper extremities. Twelve months after the procedure, the patient is well and very satisfied. His ability in daily life activities is already equivalent to that with the prostheses.

Conclusions: This case seems to confirm that bilateral arm transplantation represents a treatment option in bilateral amputees.
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**Higher Immunogenicity of a Third Heterologous Dose With BNT262b2 mRNA Vaccine Compared to a Homologous Dose in Kidney Transplant Recipients Fully Vaccinated With Inactivated Whole-Virion CoronaVac Vaccine**

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**Purpose:** This study aims to compare the immunogenicity of a third dose of the heterologous BNT262b2 mRNA vaccine versus the homologous inactivated whole-virion CoronaVac vaccine in adult kidney transplant recipients (KTR).

**Methods:** This prospective, single-center, phase 4 interventional study included KTR aged 30-69 years, with more than 30 days of transplantation and no previous confirmed COVID-19. At the transplant center, the patients received the 3rd heterologous (BNT162b2 mRNA) or homologous dose at least four weeks after the standard two-dose schedule of the CoronaVac vaccine. Antibody response immediately before and after the 3rd dose was assessed by the AdvizeDx SARS-CoV-2 IgG II assay. For those positive assays, neutralizing anti-SARS-CoV-2 antibodies were evaluated by the cPass™ SARS-CoV-2 Neutralization Antibody Detection Kit.

**Results:** There were 307 patients in the heterologous group and 777 in the homologous group. KTR in the heterologous group were older (median age 54 vs. 50 years, p<0.0001), with a lower prevalence of diabetes (7% vs. 11%, p=0.032), lower percentage of deceased donors (60% vs. 68%, p=0.006) and longer time since transplant (median 11 vs. 6 years, p<0.0001). Immediately before the 3rd dose, seroprevalence for IgG antibodies (36% vs. 34%, p=0.597) and the median antibody titers among those seroprevalent (246 AU/mL vs. 268 AU/mL, p=0.279) were similar. At a median of 25 days after the heterologous and 35 days after the homologous 3rd dose vaccine, seroconversion rate was higher in the heterologous group (49% vs. 32%, p<0.0001), resulting in a higher seroprevalence rate (67% vs. 55%, p=0.0003). Overall, 42% remained seronegative after the third dose. In addition, the median antibody titers after booster among those seroprevalent patients were higher in those in whom the 3rd heterologous vaccine was administered (7,771 AU/mL vs. 599 AU/mL, p<0.0001). The analysis of the neutralizing activity is ongoing.

**Conclusion:** This prospective interventional study suggests that a third heterologous dose is associated with a higher seroconversion rate and median antibody titers compared to a homologous dose in kidney transplant recipients fully vaccinated with inactivated whole-virion CoronaVac vaccine. In addition, 42% of subjects did not produce a humoral immune response after the third dose, urging the development of alternative strategies.

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**T-Cell Cytokine Profiles After mRNA-1273 COVID-19 Vaccination in Kidney Patients**

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**Background:** T-cells are fundamental in the control and clearance of viral infections and contribute to protective immunity by long-term immunological memory. The mRNA-1273 COVID-19 (Moderna) vaccine induces durable SARS-CoV-2 Spike (S) specific CD4+ and CD8+ T-cell responses. However, little is known about the phenotype of these S-specific T-cells over time in kidney patients with a potentially disturbed immune system. Here, we investigated the cytokines produced by T-cells obtained from mRNA-1273 vaccinated kidney patients after ex vivo stimulation.

**Methods:** Patients on dialysis (n=38), with chronic kidney disease (CKD, n=37), kidney transplant recipients (n=67) and controls (n=42) were vaccinated twice with the mRNA-1273 COVID-19 vaccine. Whole blood obtained pre-vaccination, and 28 days and six months after second vaccination, was stimulated with peptides covering the S protein in a commercially available IFN-γ release assay (QuantiFERON, QIAGEN). After stimulation, cytokines (IL-2, 4, 5, 6, 9, 10, 13, 17A, 17F, 22, IFN-γ and TNF-α) were measured in plasma by a multiplex bead assay and ELISA (IL-21). Patients were clustered at 28-days after second vaccination to identify cytokine production profiles via unsupervised clustering.

**Results:** After ex vivo stimulation with peptides covering the S protein a specific IFN-γ, IL-2, IL-5, and IL-13 response was found in all cohorts. Particularly, the Th1 cytokines (IFN-γ, IL-2) could still be detected six months after vaccination. Clustering analysis revealed no difference in cytokine profile between kidney patients and controls. Cytokine production was significantly lower in kidney transplant recipients compared to the other cohorts at 28 days and six months after vaccination (p<0.01). However, S-specific T-cell responses were still detectable in 79% of kidney transplant recipients based on the production of IL-2.

**Conclusion:** Our study shows that after mRNA-1273 COVID-19 vaccination, kidney transplant recipients have fewer S-specific T-cells, based on a multiplex cytokine assay. However, we were able to detect cytokines produced by SARS-CoV-2-specific T-cells even after six months in 79% of the kidney transplant recipients.
Introduction: Coronavirus 19 disease (COVID-19) in solid organ transplant recipients (SOT) is associated with increased morbidity and mortality. The WHO recommends vaccination as a primary prevention tool. We evaluate the safety and generation of Ab Anti-Spike in SOT patients at 28 and 90 days after Covid 19 vaccination schedule.

Methods: This is a Multicenter prospective study in SOT with a complete vaccination schedule who agreed to participate in the study. Demographic, vaccination schedule, adverse events and transplant variables were collected. Anti-spike antibodies were evaluated by the COVIDAR-IgG method at the Universidad de Buenos Aires School of Medicine. 

Results: 244 SOT patients were included from September 2021 to February 2022. Median age was 50 (IQR 41-61, women 47%). Transplant type: 62.1% kidney, 14.5% cardiac, 15.6% liver, 0.6% pancreas, kidney-pancreas 5.3% and 1.6% lung. Decreased donors 70%. The median time since transplantation to vaccination was 72.3 months (IQR 30.6-140). Only 10.3% of patients had developed rejection one year prior to vaccination and 3.3% of patients rejected post-vaccination. 146 ptes (63.3%) had triple immunosuppressive maintenance regimen (steroids + calcineurin inhibitors (ICN) + antiproliferatives), 46 pts (19.8%) received double regimen without steroids and 12 patients 19.8% (received double regimen without steroids and 12 patients). Results: 149 patients completed 3 congruent mRNA vaccines and antibody levels pre- and post-dose 3 (D3) were included. Those who reported a prior COVID-19 diagnosis or used belatacept were excluded. The latest anti-spike antibody level collected between the second (D2) and third dose (D3) was compared to the antibody level at 1 month post-D3. Samples were tested with Roche Elecsys Anti-Sars-CoV-2 enzyme immunoassay (EIA) (positive ≥0.8 U/mL) or EUROIMMUN EIA (positive ≥1 AU).

Conclusion: LT recipients that were positive or negative pre-D3 had an excellent response to a third dose of mRNA vaccine, which is beyond what has been shown in other solid organ transplant recipients. Investigation in immunogenicity remains essential to protect vulnerable groups and guide policy.
A Prediction Model for Antibody Response to Three Vaccines Against SARS-CoV-2 Among Solid Organ Transplant Recipients

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Background: Solid organ transplant recipients (SOTRs) show impaired immune response to SARS-CoV-2 vaccines. A prediction model for immune response to SARS-CoV-2 vaccines could enable targeted antibody monitoring and vaccine dose adjustments in SOTRs during potential epidemic/endemic circulations of SARS-CoV-2.

Methods: We studied 782 SOTRs recruited from across the United States who received a 3-dose series of SARS-CoV-2 vaccines and underwent serologic testing for SARS-CoV-2 antibodies between 2-5 weeks after the third dose. We used gradient boosting and logistic regression to create prediction models for positive antibody response based on demographic, transplant-related, and immunosuppression-related clinical factors.

Results: Overall, 643 (82.3%) SOTRs had positive antibody responses. The gradient boosting model predicted positive antibody response with moderate accuracy (C-statistic, 0.790). The influential predictors of positive antibody response were mycophenolate avoidance (variable importance, 43.0%), longer time since transplant (31.2%), and corticosteroid avoidance (11.9%). The logistic model showed similar prediction accuracy (C-statistic, 0.790). Mycophenolate use (aOR, 0.07 [95% CI, 0.02-0.16]), corticosteroid use (aOR, 0.39 [95% CI, 0.24-0.61]), and time since transplant (per year; aOR, 1.10 [95% CI, 1.06-1.15]) showed significant association with positive antibody response.

Conclusion: Antibody response to a 3-dose SARS-CoV-2 vaccine series could be predicted with moderate accuracy in SOTRs. This prediction model could identify SOTRs with higher risks that warrant additional vaccine doses and antibody monitoring.

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Multicenter Study to Determine the Immune Response to the Vaccine Against SARS COV-2, in Patients With Chronic Kidney Disease on Dialysis and Kidney Transplants

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Introduction: In Chile, mass vaccination was carried out, prioritizing risk groups for age and comorbidity, applying biannual vaccine boosters. As our knowledge, there are no studies evaluating the humoral and cellular response after the third booster dose in transplantation and dialysis.

Materials and Methods: Multicenter, prospective study in 100 adult patients on hemodialysis (HD) and kidney transplant (KT) recipients were evaluated. Blood samples were taken at the first visit (120 days after the second vaccination - BNT162b2 or SinoVac) and at the second visit (30 days after the 3rd vaccination - BNT162b2). ELISA against IgG Spike SARS-CoV-2 was performed to evaluate humoral response in a total of 47 HD and 53 KT patients. To evaluate cellular response, peripheral mononuclear cells from patients were stimulated with SARS-CoV-2 pool peptides, and IFN-g-secreting cells and SARS-CoV-2-specific T cell response was performed using ELISPOT and flow cytometry, respectively. Cellular immune response was performed in 31 HD and 32 KT patients. Positive cellular immune response was defined as more than 20 spots forming counts (SFC)/million cells and/or percentage of IFN-g+ CD4+ or CD8+ T cells.

Results: After analysis, only statistically significant differences, were found in mean age (in years) of 68.9 ± 13.5 vs 54 ± 12.7 (p<0.0001); kind of work (face-to-face vs homework) 85.1% vs 64.2% (p = 0.02); and in the Charlson Score 6±2.7 (points) vs 4±2.1 when comparing the HD and the KT patients, respectively. The first and second vaccine, was in HD patients mainly Coronavac (88%), while KT patients received BNT162b2 in 69%. The third vaccination, was in all cases with BNT162b2. At first visit, the seroconversion rate was 74% in HD and 48% in KT patients (p=0.001). In KT patients, a seroconversion of 13.4% was observed with Coronavac vs. 64.7% with BNT162b2 (p=0.001) (Figure 1).

Positive cellular immune response was found in 80% of KT vs 65% of HD patients after second dose. A significant higher CD8+-SARS-CoV-2-specific memory T cells were found in KT patients vaccinated with BNT162b2 as compared to Coronavac (Figure 2). At second visit, a seroconversion was observed in 97.4% HD and 94.3% in KT patients (p<0.0001). In KT patients, a seroconversion of 13.4% was observed with Coronavac vs. 64.7% with BNT162b2 (p=0.001) (Figure 1).

Conclusion: Although the humoral response with two doses of the SARS-CoV2 vaccine was poor in transplant patients, especially in those who received the Coronavac vaccine, 83% of patients had cellular immune response. Better cellular and humoral responses with BNT162b2 vaccine were found. There was a significant increase of humoral immune response with the 3rd dose. Altogether, three doses scheme including BNT162b2 are recommended for kidney transplant and hemodialysis patients.

Sociedad de Nefrologia de Chile. Sociedad de Trasplante de Chile. Fundación Pro Salud Renal.
Abstracts

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Should I Have a Transplant? Using Flexible Parametric Models To Predict Survival After Kidney Transplant Waitlisting

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Background: The Cox proportional hazards model is commonly used to compare survival between the waiting list (WL) and after deceased donor kidney transplantation (TP). However, the Cox model only allows estimation of relative but not absolute survival. Flexible parametric models (FPM) solve this by modelling the baseline hazard which enables the creation of an absolute survival prediction for individuals with different characteristics.

Aims: To develop FPMs for predicting survival on the waiting list versus deceased donor kidney transplantation.

Methods: Using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry, we included Australian adults waitlisted for first kidney-only deceased donor transplants over 2007-2020. We developed FPMs for waitlist and post-transplant survival. Covariates were decided using backwards elimination and the baseline hazard function was modelled using cubic splines.

Results: 7552 patients were included in this analysis: 5429 (72%) received a deceased donor kidney transplant. The models were adjusted for age, gender, primary kidney disease, dialysis duration, comorbidities, and smoking status. The FPM allowed calculations of individual mean life expectancy (Figure 1).

Example 1, TP: 69 years (95% CI 63-75), WL: 41 years (95% CI 15-67), Difference: 28 years.
Example 2, TP: 17 years (95% CI 13-22), WL: 9 years (95% CI 7-10), Difference: 8 years.
Example 3, TP: 4 years (95% CI 3-6), WL: 4 years (95% CI 3-5), Difference: 0.5 years.

Conclusions: FPM can predict risk for patients on the kidney transplant waitlist. For the first time, this enables absolute survival prediction, to help patients and clinicians understand the likely outcomes of transplantation vs remaining on dialysis. The next step will be model validation and incorporation of quality-of-life utilities.

Figure 1. Percentage of patients with positive humoral and cellular immune response 4 months after two doses and 1 month after third dose. HD: hemodialysis patients; TR: kidney transplant patients.

Figure 2. CD8\(^{+}\)IFN-\(\gamma\)\(^{+}\) memory T cells in kidney transplant patients with two doses of coronavac or BNT162b2 and third dose of BNT162b2. B:BNT162b2; C:Coronavac.

Individualised predicted survival

Parameteric survival models

Post Transplant Survival ––– Waiting list survival

Example 1

Example 2

Example 3
Long-term Consequences of Kidney Donation 15 – 30 Years Post-donation. an Experience From a Dedicated Donor Clinic in a Low-Income Country

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Introduction: In low-income countries, living donors provide the majority of the kidneys for transplantation. Long-term follow-up of donors is important to maximize donor safety and prevent the adverse consequence of donation. In this study, we report long-term outcomes of kidney donors 15 years and beyond after donation.

Method: In an observational cohort study, 1093 kidney donors whose post-nephrectomy period exceeded 15 to >30 years were followed-up yearly in a dedicated clinic from 1985 - 2020. Each visit-included history, physical exam, blood tests for renal, lipid, glucose profiles and 24-hour urine for proteinuria and creatinine clearance. Preventive intervention was undertaken for new consent clinical conditions. All treatments including medication were given free of cost to all donors. The donors were divided into four groups, Group 1, nephrectomy duration (15-20 years), Group 2, (21-25 years), Group 3, (26-30 years) and Group 4, (>30 years). Descriptive statistics were used using SPSS version 22.0.

Results: In the period 1985 – 2020, 1093 donors had a post-nephrectomy period of ≥15 years. The mean age at donation was 34.3±9.8 years with a Male to Female ratio of 1.2:1. The mean post nephrectomy period was 21.7±4.2 years (range 15.1 – 35.1 years). The mean age at the last follow-up in Group-1 was (49.5±10.2 years), Group-2 (55.6±10.9 years), Group-3 (59.7±11.3 years) and Group-4 (62.0±9.2 years). Overall age range at last follow-up was (33-90 years). Overall Creatinine Clearance in ml/min/1.73m2 was 109.8±22.3 pre-donation, 83.96±18.85 at 1 year, 83.03±21.27 at 15 years, 77.5±22.79 at 25 years and 75.42±16.18 at 30 years. Mean Creatinine Clearance was 84.4±20 in Group-1, 80.2±21 in Group-2, 75.6±19.1 in Group-3 and 74±14 in Group-4. Protein Excretion mg/24-hour was <150 in 72%, 76%, 71% and 66% respectively in Group 1-4. Overall, of 1093 donors 4% had Protein Excretion of > 1000 mg/24-hour at post-donation period of 21.5±5.2 years. New-onset diabetes was found in 2.9% and hypertension in 5%. ESRD and mortality beyond 15 years was 0.87/10,000 person-years and 2.63/10,000 person-years respectively.

Conclusion: Donor nephrectomy has minimal adverse effects on the overall health status of donors 15-30 years post-donation. Regular follow-up identified the new-onset of disease and allowed intervention that may have prevented adverse outcomes. Donor clinic has given confidence to the community and enhanced living-related donations.

Institutional Funding.

Characteristics, Demographics and Outcomes of Kidney Transplant Recipients With Extreme Dialysis Vintage > 10 Years. A National UNOS Database Review 2000-2021

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Introduction: Prolonged dialysis times (DT) have been associated with inferior outcomes. Nevertheless, rarely suitable candidates with extreme dialysis vintage are transplanted. We aimed to review the characteristics, demographics and outcomes of such patients.

Methods: We used United Network for Organ Sharing registry data to assess outcomes for patients who were on dialytic therapy for a minimum of 10 years, who received a kidney alone transplant from Jan 1 2000 – Dec 31 2021. Pediatrics, multi-organ transplants and those without a confirmed dialysis start date were excluded.

Results: During the study period, a total of 361,029 kidney alone transplants were performed, of which 70.3% were patients who were on dialysis at the time of transplant. Out of the 253,841 dialysis patients, transplanted, 962 (0.37%) patients met our criteria. The majority of transplants (78.7%) in these 962 cases were performed after Dec, 2014 when the new KAS allocation which credits waitlist time from chronic dialysis initiation was implemented. There was no difference in graft survival for race, gender, but DM and DGF were independent predictors of inferior survival (p<0.05).

Conclusions: The present study is the first to look at the granular details of this unique group of patients who receive a transplant after a minimum of 10 years of dialysis. Although outcomes may be somewhat inferior to standard outcomes of patients with shorter dialysis times, carefully selected candidates can still have reasonable successful outcomes.

Recipient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age at Time of Transplant (yrs)</td>
<td>49.9+/–10.5 (18-75)</td>
</tr>
<tr>
<td>Race (AA/Whites/Hispanics) (%)</td>
<td>41.9/21.1/24.7</td>
</tr>
<tr>
<td>Gender (M/F) (%)</td>
<td>53.5/38.5</td>
</tr>
<tr>
<td>Re-Transplants (%)</td>
<td>38.5</td>
</tr>
<tr>
<td>Deceased Donor/ Living Donor Transplants (%)</td>
<td>97.3/2.7</td>
</tr>
<tr>
<td>Etiology of ESRD (DM/HTN/Other) (%)</td>
<td>24.8/20.7/54.5</td>
</tr>
<tr>
<td>CPRA (0-20, 20-80, 80-98, 98-100) (%)</td>
<td>31.8/19.6/12.7/35.9</td>
</tr>
<tr>
<td>Zero Mismatch (%)</td>
<td>5.7</td>
</tr>
<tr>
<td>PVD (%)</td>
<td>5.2</td>
</tr>
<tr>
<td>Median/Dialysis Time (yrs)</td>
<td>12.4 (10-32)</td>
</tr>
<tr>
<td>Dialysis Time (10-15yrs/ 15-20yrs/ &gt; 20 yrs) (%)</td>
<td>76.7/16.4/ 6.8</td>
</tr>
<tr>
<td>Donor Characteristics</td>
<td></td>
</tr>
<tr>
<td>Mean Donor Age (yrs)</td>
<td>36.4+/–13.9 (1-69)</td>
</tr>
<tr>
<td>Donor Race (Whites/AA/Hispanics) (%)</td>
<td>52/18.6/22.6</td>
</tr>
<tr>
<td>Donor Gender (M/F) (%)</td>
<td>61.9/38.1</td>
</tr>
<tr>
<td>DCD (%)</td>
<td>16.4</td>
</tr>
<tr>
<td>ECD (%)</td>
<td>6.3</td>
</tr>
<tr>
<td>KDPI Median</td>
<td>38</td>
</tr>
<tr>
<td>KDPI &gt; 85 (%)</td>
<td>1.8</td>
</tr>
<tr>
<td>Donor HTN/ DM (%)</td>
<td>21.5/4.3</td>
</tr>
<tr>
<td>Median Cold Ischemia Time (hrs)</td>
<td>16</td>
</tr>
<tr>
<td>Kidneys Pumped (%)</td>
<td>34.5</td>
</tr>
<tr>
<td>Donor PHS Increased Risk (%)</td>
<td>15</td>
</tr>
<tr>
<td>Transplant Outcomes</td>
<td></td>
</tr>
<tr>
<td>DGF (%)</td>
<td>34.7</td>
</tr>
<tr>
<td>Acute Rejection within 1 year (%)</td>
<td>9.8</td>
</tr>
<tr>
<td>Mean Length of Stay (days)</td>
<td>7.7+/–9.1</td>
</tr>
<tr>
<td>Patient Death within 30 days n (%)</td>
<td>8 (0.8)</td>
</tr>
<tr>
<td>Graft Failure Within 30 days n (%)</td>
<td>25 (2.5)</td>
</tr>
<tr>
<td>Graft Survival (%) 1yr/ 3yr/ 5yr/ 10 yr</td>
<td>92/80/70/41</td>
</tr>
<tr>
<td>Patient Survival (%) 1yr/ 3yr/ 5yr/ 10yr</td>
<td>96/88/80/50</td>
</tr>
</tbody>
</table>
Clinical Outcomes of Simultaneous Heart Liver Kidney Transplant Recipients, Single Center Experience

Juhi Bhargava, Sambhavi Krishnamoorthy, Yousuf Kyese. Transplant Nephrology Medicine, University of Chicago, Chicago, IL, United States.

Introduction: Multiorgan dysfunction involving the kidneys is not uncommon in patients with end stage heart and liver disease. Simultaneous heart-liver-kidney transplants (HLK) are less commonly performed than simultaneous heart-kidney or liver-kidney transplants due to the complex nature of the surgery and challenges with patient selection. 19 HLK were performed in the US from 2008 to 2020, out of which 8 were performed at our center. Given the limited availability of organs for transplant and the lack of standardized qualifying criteria for these patients, it is imperative to understand the factors involved in better outcomes, to optimize utilization of scarce resources.

Method: We performed a retrospective review of all HLK recipients at the University of Chicago medical center between 2008-2020 using Epic EMR. We evaluated their renal outcomes, infection rates, number of hospitalizations, and mortality over a 12-month period post transplantation.

Results: Baseline characteristics are summarized in the table. 4(50%) were between the ages of 50-64, 2(25%) were between the ages of 35-49, and 2(25%) were between the age of 18-34. Four (50%) were Caucasians, 3(37.5%) were African Americans, and 1(12.5%) was Asian Indian. 6 (75%) had pre-transplant GFR above 60 ml/min, 3 (37.5%) were between 45-60 ml/min, and 2 (25%) were below 45 ml/min. All had GFR above 50 ml/min at 3 months post-transplant, out of which 3(37.5%) were African Americans, and 1(12.5%) was Asian Indian. 6 (75%) had Kidney Donor Profile Index (KDPI) below 50%.

Conclusions: Our experience suggests that with careful selection of patients, simultaneous HLK can lead to successful patient outcomes at one year post transplantation. Longer follow up of these patients is needed to define long term allograft function and patient survival which will help to standardize selection and allocation criteria of this subset of patients.

Transplant Candidate Outcomes After Accepting Sclerotic Kidneys in the United States, 2015-2018

Laura Zeiser, Dorry L Segel, Allan B Massie. Department of Surgery, Johns Hopkins School of Medicine, Baltimore, MD, United States; Department of Surgery, NYU Langone School of Medicine, New York, NY, United States.

Introduction: Waitlist candidates who accept the offer of a sclerotic kidney are faced with increased risk of delayed graft function and graft loss, but candidates who decline must wait for a future offer that could involve additional risks or may never materialize. To investigate the potential benefits of accepting a sclerotic kidney, we compared patient mortality between recipients of sclerotic kidneys and waitlist candidates who declined offers of the same kidneys.

Methods: Using national registry data from the United States (SRTR), we identified all offers from deceased donors with at least 20% glomerulosclerosis of both kidneys, 2015-2018. We compared demographic and clinical characteristics of sclerotic kidney recipients to waitlist candidates who declined the offers. Patients were followed from the time of offer until death or administrative censoring on March 31, 2021. An odds-weighted Cox proportional hazards model including candidate age, sex, race, education, insurance type, BMI, primary diagnosis, time on dialysis, calculated panel reactive antibody (cPRA), ABO type, previous malignancy, previous transplant, serum albumin, and peripheral vascular disease was used to compare mortality between the two groups.

Results: 28,463 offers of sclerotic kidneys were made to 17,467 patients, among whom 245 accepted and received a sclerotic kidney. 207 candidates accepted the first offer of a sclerotic kidney, while 38 accepted a subsequent offer. Compared to their counterparts, sclerotic kidney recipients were older (p<0.001), less likely to be male (60% vs. 66%, p=0.04) or privately insured (28.7% vs. 41.5%, p<0.001), have cPRA >80% (14.3% vs. 5.1%, p<0.001), have peripheral vascular disease (16.7% vs. 8.5%, p<0.001) (Table 1). Weighted cumulative incidence of mortality following the offer was 6%, 13%, and 22% among recipients and 4%, 16%, and 27% among comparable patients who declined the offer at 1, 3, and 5 years, respectively (Figure 1). Relative risk of mortality did not vary between those who accepted the sclerotic kidney and those who declined (HR=0.81, 95% CI=0.61-1.08).

Conclusions: Offers of kidneys from donors with >20% sclerosis of both kidneys, those who accept do not appear to receive any survival benefit. However, as organ availability varies widely by geographic region in the U.S., so too may the advantages of accepting or declining these organs. Decisions regarding offers of sclerotic kidneys should be considered carefully in the context of organ availability.

Table 1. Characteristics of candidates who declined or accepted offers of sclerotic kidneys in the United States, 2015-2018.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Declined Offer (N=17220)</th>
<th>Accepted Offer (N=245)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at offer, median (IQR)</td>
<td>57 (48, 65)</td>
<td>61 (53, 68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>11424 (66.3%)</td>
<td>147 (60.0%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>5483 (31.8%)</td>
<td>87 (35.5%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Black</td>
<td>5411 (31.4%)</td>
<td>64 (26.1%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>4155 (24.1%)</td>
<td>56 (22.9%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2171 (12.6%)</td>
<td>38 (15.3%)</td>
<td></td>
</tr>
<tr>
<td>Insurance type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>7117 (41.5%)</td>
<td>70 (28.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Public</td>
<td>9998 (58.4%)</td>
<td>174 (71.3%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>19 (1.0%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>ABO type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>6500 (38.5%)</td>
<td>86 (35.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>B</td>
<td>876 (5.1%)</td>
<td>34 (13.9%)</td>
<td></td>
</tr>
<tr>
<td>AB</td>
<td>505 (2.9%)</td>
<td>4 (1.6%)</td>
<td></td>
</tr>
<tr>
<td>O</td>
<td>9165 (53.5%)</td>
<td>120 (49.2%)</td>
<td></td>
</tr>
<tr>
<td>Maximum cPRA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-20%</td>
<td>12887 (73.7%)</td>
<td>168 (68.8%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>20-40%</td>
<td>3372 (19.6%)</td>
<td>42 (17.1%)</td>
<td></td>
</tr>
<tr>
<td>40-60%</td>
<td>1162 (6.7%)</td>
<td>35 (14.3%)</td>
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</tr>
<tr>
<td>Primary diagnosis</td>
<td></td>
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<tr>
<td>Diabetes</td>
<td>6579 (38.5%)</td>
<td>93 (38.1%)</td>
<td>0.9</td>
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<tr>
<td>Hypertension</td>
<td>4369 (24.4%)</td>
<td>55 (22.5%)</td>
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<tr>
<td>Glomerular disease</td>
<td>1217 (7.1%)</td>
<td>19 (7.8%)</td>
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</tr>
<tr>
<td>Other</td>
<td>5131 (30.0%)</td>
<td>77 (31.6%)</td>
<td></td>
</tr>
</tbody>
</table>
Impact of Left Ventricular Ejection Fraction and Previous Cardiac Revascularization on Patient and Graft Survival in Kidney Transplant Receipts

Dominic Amara1,2, Miguel Nunez2, Justin Parekh3, David Foley4, Stuart Greenstein5, Ryutaro Hirose6.
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Background: Single center studies have implicated baseline left ventricular ejection fraction (LVEF) and baseline coronary artery disease as strongly associated with post-kidney transplant graft and patient survival, including in limited multivariate models. However, the United States’ Scientific Registry of Transplant Recipients (SRTR) does not directly include any cardiac variables as part of its risk adjustment model, raising the question of whether the current SRTR model fairly risk adjusts potential recipients.

Methods: This study used the novel prospective United States National Surgical Quality Improvement Program (NSQIP) Transplant database to assess the impact of LVEF and pre-transplant revascularization on post-transplant outcomes in deceased donor renal transplantation (DDRT). Recipients from 2017-2019 were identified and stratified by LVEF into <50 and 50+ categories. A separate analysis stratified patients into if they had received pre-transplant revascularization, defined as either coronary bypass surgery or percutaneous intervention. Post-transplant outcomes were assessed.

Results: A total of 2377 DDRT recipients were included from 29 centers. Mean follow up was 200 days. Only 4.8% had LVEF<50 at transplant, while 13.3% had undergone cardiac revascularization prior to transplant. There were several baseline differences between patients who did and did not have previous revascularization.

Previous revascularization was associated with increased risk of requiring cardiac CPR (1.3 vs 0.1%, p=0.002), organ space surgical site infection (3.8 vs 1.1%, p=-0.001), delayed graft function (39.2 vs 28.3%, p<0.001), requiring dialysis at last follow up (5.7 vs 3.9%, p<0.001), myocardial infarction (4.4 vs 0.8%, p<0.001), pneumonia (3.2 vs 1.1%, p=0.011), recatheterization (14.2 vs 8.2%, p=0.002), sepsis (4.1 vs 1.7%, p=0.018), septic shock (1.3 vs 0.3%, p=0.036), UTI (10.1 vs 6.1%, p=0.023), and longer ICU stay (0.86 vs 0.47 days, p=0.004). In univariate analysis, previous revascularization was associated with increased hazard of death (HR 2.4, p=0.02) but not graft loss (HR 1.3, p=0.52). In a multivariate model including previous revascularization and existing SRTR variables (age, diabetes, peripheral vascular disease, albumin, KDRI) as predictors, previous revascularization was related to a higher hazard of death (HR 1.43) however this was not a statistically significant finding (p=0.42).

Conclusions: We conclude that in the DDRT in patients with previous cardiac revascularization is much more common (13.3%) than in those with LVEF<50 (4.8%). We also demonstrate that previous cardiac revascularization is a powerful predictor of both patient survival and several post-transplant complications. However, we also show that existing variables (e.g. diabetes, PVD, age) in the SRTR risk stratification model largely capture the impact of previous cardiac revascularization on patient survival at least in the early follow up period.
To Study Effect of Renal Transplantation on Cardiac Functions in CKD Stage 5 Patients

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Introduction: In CKD patients Cardiac disorders like left ventricular hypertrophy (LVH), left ventricle (LV) dilatation, reduced LV fractional shortening and diastolic dysfunction are very common. These cardiac abnormalities continues to progress as CKD progresses even in the first year of dialysis. We planned a study to evaluate echocardiographic changes in CKD stage 5 patients after renal transplantation by periodic echocardiographic parameters measurement in pre and post transplantation period in Indian population.

Methods: 51 consecutive renal transplant recipients (37 males, 14 females), undergoing live donor renal transplantation were taken in the study after written consent. Four echocardiographic parameters were assessed ie, 1) Left ventricular ejection fraction (LVEF), 2) Grade of diastolic dysfunction, 3) Left ventricular wall thickness and 4) Left ventricular end diastolic diameter, both pre-transplant and post-transplant. The post-transplant echocardiographic evaluation was done between 6 to 18 months of transplantation. Besides the clinical parameters, the biochemical parameters, immunosuppressives and other medication requirements were recorded.

Observation: Pre Tx (Transplant) average systolic BP of 147.05±14.32 mm Hg improved in Post Tx period to 126.67±18.07 with P value- < 0.0001. Pre Tx average diastolic BP was 89.41±7.85 mm Hg which also improved in Post Tx period to 76.67±11.07 (P value- <0.0001). Average pre Tx LVEF was found to be 60.74±7.26%. In post Tx period, it improved significantly to 65.02±4.31%, (p value < 0.0001). An increase of LVEF ≥ 5% of pre-Tx level was considered to be significant improvement in this study. All 11(100%) patients with pre transplant LVEF < 54%, showed ≥ 5% improvement in LVEF post transplantation. We also noticed that patients with pre Tx normal LVEF (>55%), but BP uncontrolled, after transplantation, were trending towards lower improvement of LVEF than those with BP controlled. Of 44 patients, having some grades of diastolic dysfunctions pre-Tx, 21 patients(47.7%) had improvement whereas 18 patients(40.90%) had no improvement and 5 patients(11.36%) had further diastolic functions deterioration. In this study, average interventricular wall thickness was 1.22±0.18 cms in pre Tx assessment and it decreased to 1.15±0.15 cms (p value= 0.01). Similarly, average pre Tx LV posterior wall thickness of 1.19±0.18 cms was reduced in post Tx period to 1.14±0.14 cms (P value = 0.027).Average pre Tx LVEDD was found to be 4.9± 0.52 cms and in post Tx was 4.47± 0.42 cms. Thus it improved after transplantation significantly (p value<0.0001).

Conclusion: Our study suggests Kidney transplantation brings in significant improvement in Systolic BP, Diastolic BP, IVS wall thickness, LV posterior wall thickness, LV Ejection Fraction, LV End diastolic diameter and LV diastolic function post renal transplantation.
Determining the Presence of torque teno virus in kidney transplant patients

Patricia Bonaventura1, Martín Aijzenzlos2, Raúl Julieta3, Cisterna Daniel4, Daniela Beltrán5, Michelle Parejas2, Marcelo Carpio2, Lourdes Pantelli2, Miguel Raño2, Fernando Margulis2, Elena Maiolo5, Ruben Schiavelli1.

1Chief Of Nephrology and Renal transplant, Hospital General de Aguad; Cosme Argerich, Caba, Argentina; 2Division of Nephrology and Renal transplantation, Hospital General de Aguad Cosme Argerich, Caba, Argentina; 3Servicio de Neurovirosis, Departamento de Virologia, Instituto Nacional de Enfermedades Infecciosas, ANLIS “C.G. Malbrán”, Caba, Argentina; 4Uniforme de Infectología, Hospital General de Aguad Cosme Argerich, Caba, Argentina.

Introduction: Introducing immune monitoring strategies in the clinical practice when following up transplant patients may minimize infectious and immunological events by individualizing treatments. One of the agents explored in this monitoring is torque teno virus (TTV). TTV is a small non-enveloped, circular single-strand DNA virus of the Anello virus family. Primary infection occurs at an early age, followed by a latent infection, mainly in peripheral blood mononuclear cells with a prevalence of over 90%. Thus far, it has not been possible to prove any directly attributable pathogenic effect in human beings. Several studies have shown that reactivation of latent infection by anelloivirus is more frequent in patients with chronic debilitating diseases, cancer, HIV infection, and in organ transplant recipients. TTV is diagnosed with a real-time PCR assay (rt-PCR), and cycle threshold (Ct) values of an RT-PCR assay refer to the number of cycles needed to amplify viral DNA to reach a detectable level.

Objective: To describe the behavior of TTV Ct values in kidney transplant patients with infections (iKTPs), using stable kidney transplant patients (sKTPs) and healthy individuals (HIs) as control groups.

Methods: A single plasma sample of each individual from the three groups under study was processed. DNA was extracted with silica columns and the presence of TTV was subsequently determined by means of an rt-PCR using a specific probe (TaqMan chemistry). Student’s t-test was used, analyzing the Ct values for each group; a p-value less than 0.05 was considered statistically significant.

Results: Fifty-seventy percent of the Ps studied were women. The average age of iKTPs and sKTPs was 54 and 50 years, respectively. The period of time after transplantation was 27 months (4-57) for iKTPs and 112 months for sKTPs. The infections of iKTPs were:

- iKTPs 1 - Pulmonary cryptococcosis/COVID-19/CMV
- iKTPs 2 - KPC urosepsis/Strongyloidies stercoralis colitis/pulmonary nocardiosis/cutaneous aspergillosis
- iKTPs 3 - Meningeval cryptococcosis/Clostridium difficile
- iKTPs 4 - CMV/ Meningeval cryptococcosis/MISSA Skin and soft-tissue infection/ Respiratory-related sepsis
- iKTPs 5 - CMV/Kpnc-KPC urosepsis/ESBL E. faecalis + Candida UTIs

A total of 23 plasma samples were processed: 5 iKTPs, 7 sKTPs and 11 HIs. Seventy-eight percent (18 Ps) tested positive for TTV. Positivity for the iKTP group was 100%, for sKTPs, 71% and for HIs, 73%. The average Ct values observed were 22.6 for the iKTP group, 30.1 for sKTPs and 31 for HIs. When comparing the Ct values for iKTPs vs. sKTPs and for iKTPs vs. HIs, we obtained P = 0.013 and 0.003, respectively.

Conclusions: There were no significant differences in gender, age at transplantation, and number of follow-up periods between the patients without or with DGF. Median circulating lymphocyte value was significantly higher in DGF when compared to the non-DGF patients (p<0.05). Furthermore, the median value for SII, NLR and PLR were significantly lower in DGF when compared to the non-DGF patients (49.4% vs 40.3%, p=0.004; 73.9% vs 39.0%, p=0.003; and 82.6% vs 49.4%, p=0.004).

Conclusions: In our study, pre-transplanted low SII, NLR and PLR was inversely associated with DGF. Therefore, these novel and non-invasive inflammatory biomarkers may conduce to an early prediction of DGF in kidney transplant recipients.
Microvascular Injury With Macrophage, Neutrophil, And Hla-dr Positive Inflammatory Infiltrate, either in dsa Positive or Negative abmr, Determines the Prognosis in Renal Allografts

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Introduction: Antibody-mediated rejection (ABMR) has well-defined histomorphological lesions, like linear C4d staining or microvascular inflammation (g + ptc) ≥ 2 in peritubular capillaries (PTCs). Although these histologic features of ABMR (ABMRh) are usually compatible with donor-specific antibodies (DSA), it is demonstrated that recipients can develop ABMR without the presence of DSAs. Indeed, DSA can not be found in 40–60% of patients with marked microvascular inflammation (MVI). We aimed to investigate the relationship between PTC macrophage (M), neutrophil, and HLA-DR positive cell infiltration with variable clinical presentations of ABMR.

Methods: A total of 125 patients with acute ABMR were categorized into four groups; Group 1: DSA (+) ABMR, Group 2: DSA (-) ABMR, Group 3: DSA (+) mixed rejection (ABMR+vascular rejection), and Group 4: DSA (-) mixed rejection. The degree of the glomerular and PTC macrophage (CD68+), neutrophil, and HLA-DR positive cells was graded. The loss of HLA-DR expression in PTC endothelium was accepted as PTC destruction. The follow-up biopsies were evaluated for the development of diffuse interstitial fibrosis (IF) and transplant glomerulopathy (TG).

Results: The type of ABMR showed a significant correlation with PTC C4d expression, the presence of TMA, PTC destruction, microvascular (PTC and glomerular) macrophage, neutrophil, and DR+ cell infiltration (p<0.01 for all). Group 3 developed the highest microvascular inflammation, PTC destruction, C4d expression, and TMA. Groups 4, 1, and 2 followed Group 3, respectively, and Group 2 showed the best outcome. Also, patients in Group 3 developed the highest and earliest IF and TG development during follow-up (p<0.01). Similarly, Groups 4, 1, and 2 followed Group 3 regarding the development of IF and TG development. PTC C4d staining intensity significantly correlated with PTC destruction and DSA positivity (p<0.001). Overall 5-year graft survival was 86%, 51%, 45%, and 26% for Groups 2, 1, 4, and 3, respectively (p<0.001). Overall 5-year graft survival was 87%, 54%, and 20% for patients with grades 1, 2, and 3 PTC destruction, respectively (p<0.001). Additionally, overall 5-year survival was 100%, 81%, and 21% for grades 1, 2, and 3 C4d depositions in PTCs, respectively (P<0.001).

Conclusion: ABMRh comprising characteristic histologic findings without detectable DSA represent a distinct phenotype with superior renal allograft survival than ABMRh with positive DSA. Additionally, PTC C4d deposition and the resulting PTC destruction were shown to significantly indicate graft failure and poor prognosis independent of the DSA positivity. Therefore, we concluded that ABMR should be divided into different subgroups for treatment, considering the presence of DSA and vascular rejection.

Meta-Analysis of Association Between TCF7L2 RS7903146 And Risk of New-Onset Diabetes After Transplantation

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Background: Single nucleotide polymorphisms may influence the risk of development of new-onset diabetes after transplantation (NODAT), a post-transplant clinical complication that is often implicated in allograft rejection and mortality. We performed a meta-analysis of association between TCF7L2 rs7903146 and risk of post-transplant diabetes mellitus.

Methods: A systematic search was conducted using PubMed and ScienceDirect electronic databases for studies published between January 2001 to January 2021. Case-control or cohort studies reporting association between NODAT (diagnosis based on American Diabetes Association [ADA] criteria) and TCF7L2 rs7903146 were included. MetaGenyo was used for meta-analysis (random effects model). Pooled odds ratios with 95% confidence intervals were reported to evaluate the strengths of association.

Results: Two reviewers independently screened for articles. A total of six case-control studies were included for full-text review and quantitative analysis after screening for eligibility. Genotypic distributions were in Hardy-Weinberg equilibrium for included studies. All papers reported statistically significant association of TCF7L2 rs7903146 for risk of NODAT, except for one study. There was moderate heterogeneity among studies (I2 = 60.6%). Pooled analysis revealed 51% odds of developing NODAT with TCF7L2 rs7903146 T allele (Allele Contrast Model: OR = 1.51, 95% CI 1.13 – 2.02, adjusted p = 0.03).

Conclusion: The present meta-analysis demonstrated association between TCF7L2 variant rs7903146 and risk of developing NODAT. This finding may have clinical implications for individuals undergoing kidney transplantation.
Preoperative Ultrasound in Assessing Deceased Donor Kidney Quality Based on Clinical Parameters in Kidney Transplantation

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We evaluated the role of functional kidney volume using donor kidney ultrasound (US) alone or in combination with other donor factors and parameters appropriate for kidney grafts in deceased donor kidney transplantation (DDKT). A total of 273 patients who underwent deceased donor kidney transplantation from 2000 to 2020 at Samsung Medical Center were enrolled after adjusting for exclusion criteria.

Estimated GFR was used to evaluate kidney function. An experienced genitourinary radiologist (*BLINDED*) with more than 7 years of experience in kidney US analyzed the stored kidney US images. Renal size, cortical thickness, parenchymal thickness, and cortical echogenicity on US were analyzed. The renal size was defined as the longest diameter on the longitudinal axis of the kidney. The cortical thickness or parenchymal thickness was measured in the upper, middle, and lower levels of the kidney, and averaged to calculate the representative cortical thickness or parenchymal thickness of each patient.

To binarize each kidney US characteristic, an optimal cut-off value for eGFR less than 30 within 1 year after KT was selected using Youden’s index from among values with a specificity above 60%.

Cox regression analysis was performed for eGFR less than 30 within 1 year after KT and graft failure within 2 years after KT. We found that all of the selected US characteristics were risk factors for eGFR less than 30 within a year after KT. The odds ratios of renal length, cortical thickness, parenchymal thickness and the product of renal length and cortical thickness were 6.417 (95% CI: 1.332-28.361, P = .020), 10.146 (95% CI: 1.934-53.217, P = .006), 6.665 (95% CI: 1.540-28.852, P = .011) and 14.700 (95% CI: 2.805-77.030, P = .001), respectively. Cortical thinning and decreased product of renal length and cortical thickness were risk factors for graft failure within 2 years after KT, with odds ratios 3.792 (95% CI: 1.006-14.295, P = .049) and 4.129 (95% CI: 1.119-15.236, P = .033), respectively. Based on these results, US evaluation of donor kidney can predict short-term prognosis after KT and can be used to facilitate deceased donor selection.

In conclusion, preoperative ultrasound of the donor kidney can be used to evaluate donor kidney function in addition to traditionally used laboratory parameters and medical history. However, the purpose of our study was not to narrow down the expanded criteria by these preoperative evaluations, but to avoid catastrophic consequences by identifying acceptable kidneys.

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**332.7**

**Ethnic Variation in Human Leukocyte Antigen Coverage by Single Antigen Testing Panels: Implications for Clinical Applications**

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**Introduction:** Modern tests for HLA antibodies usually involve single antigen reagents, but clinically significant HLA antibodies may not be detected if their epitopes are not included in the reagents. Reagents from two vendors were examined to determine antigen coverage in eight ethnic populations: Hispanic (HIS), Native American (NAM), African American (AFA), Asian and Pacific Islander (API), Middle Eastern and North Coast of Africa (MENA), European (EUR), and mixed or unknown ethnicity (UNK).

**Methods:** HLA-A, -B, -C, and -DRB1 allele frequencies of each ethnic population were determined using the Common, Intermediate, and Well Documented HLA allele catalog (v3.0). For each ethnicity, the percentage of alleles not represented in single antigen reagents from two common suppliers (Vendor 1 and Vendor 2) was calculated and compared.

**Results:** Antigen coverage between single antigen reagents from the two vendors differed depending on ethnicity and HLA locus, with a maximum differential of 14.0%. For the HLA-A locus, Vendor 1 better represents the HIS, API, and NAM populations, with 3.6%, 2.8%, and 2.2% greater representation than Vendor 2, respectively. At the HLA-B locus, the most striking difference is greater representation of the API and AFA populations by the Vendor 1 standard panel by 9.1% and 6.2%, respectively. However, Vendor 2 better represents the HLA-C alleles of all ethnic populations, with 14.0% increased coverage for the API population compared to Vendor 1. Finally, the greatest benefit in HLA-DRB1 coverage was seen in the API and HIS populations with a respectively increased coverage of 6.5% and 5.1% when the Vendor 2 panel was used. High resolution typing of 60 deceased donors showed that 28.3% of donors had at least one HLA allele that was not represented in either vendor’s reagents. Molecular modeling showed that many of these HLAs had potential epitopes that were not represented in other HLAs in the reagents.

**Conclusion:** Antibody reagents do not cover all HLA alleles and may not be sufficient in ruling out the presence of HLA antibodies, since every ethnic population has HLA antigens that are not represented in single antigen reagents. This risk is increased in non-European populations. Different vendors choose different antigens to cover, and thus have different strengths with different ethnic populations.

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**332.8**

**Optimized Use of Erythropoietin Stimulating Agents in Kidney Recipients With Post-transplant Anemia: A Prospective Randomized Controlled Trial**

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**Objectives:** Many studies suggested that chronic allograft nephropathy might progress faster in patients with PTA, but whether full correction of anemia improves renal outcomes is unknown.

**Aim of the work:** We aimed to assess the impact of full correction of chronic anemia in renal transplant recipients with stable graft function on patient and graft outcome along one year follow-up.

**Patient and methods:** We enrolled 247 kidney recipients with stable graft function to be assessed for anemia. Eligible patients were randomized to achieve target hemoglobin between 11:12 g/dl (group 1, n=183), or 13:15 g/dl (in group 2, n=64) using erythropoietin receptor stimulating agents (ESA). Monthly clinical and laboratory evaluation of kidney graft function was carried out. Quality of life was assessed at the start and 12 months.

**Results:** More females were found in group 1 (68.9%) vs. (50%) in group 2 (p=0.007), and the original disease was chronic glomerulonephritis (37.5%) followed by diabetic nephropathy (DN) (15.7%) in group 2; but DN patients predominated in group 1 (p= 0.007), and the original disease was chronic glomerulonephritis (37.5%) in group 2. More females were found in group 1 (68.9%) vs. (50%) in group 2 (p=0.005). The studied groups were comparable regarding pre-transplant co-morbidities. Most patients received thymoglobulin as induction and most of them were maintained on cyclosporine. We did not find any significant difference between the two groups concerning post-transplant diabetes, BK viremia or malignancies (p >0.05), however better graft function was observed in group 2 at 6 months (p<0.05). We found that required ESA doses were significantly higher in patients of group 1 from the 6th month. Group 1 showed higher mean albumin (p=0.003) while group 2 showed higher mean albumin (p=0.05). Graft outcome was comparable in both groups (p=0.125), but mortality cases were significantly higher in group 1 (16 cases, 8.7%) vs. 5 cases, 2.2%).

**Conclusion:** Full correction of PTA in renal transplant recipients had no positive impact on graft outcome but it was associated with better patient survival possibly due to improved cardiovascular risk.
332.9
Utility of Color Doppler Ultrasound and Contrast Enhanced Ultrasound in Predicting Kidney Transplantation Outcome: A Monocentric Study

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Background: Renal transplant is the gold standard therapy for irreversible chronic kidney disease. However, frequently the functional recovery of transplanted kidneys is deferred, configuring the clinical diagnosis of Delayed Graft Function (DGF), involving 25% of patients undergoing renal transplant and requiring at least one dialysis treatment in the first post-transplantation week. The purpose of our study is to validate the use of ultrasound for the prediction of the outcome of the graft, with the aim of setting a new predictive model for grafts outcome based on Ultrasound examination.

Methods: Our study is based on two objective endpoints, both addressed on the use of ultrasound:
□ the first endpoint was pursued through a retrospective study, involving patients who underwent kidney transplant from 2013 to 2021, subjected to Color-Doppler Ultrasounds (CDU) in their 1st, 4th day after surgery and the day of clinical dimissions;
□ the second endpoint was pursued through a prospective study, involving patients who underwent Contrast-Enhanced Ultrasounds (CEUS) in their 7th day after surgery.

The study was performed with Philips EPIQ 7 ultrasound scope (Philips Healthcare, Andover, MA) and SonoVue (Bracco Company, Milan, Italy) as contrast medium. For CDU the variables considered were upper and lower Resistive Indexes (RRI) and their average. Over CEUS, the Ultrasound Dynamic evaluation was performed for 1 minute. A 10mm side square region of interest (ROI) was defined on the superior polar renal cortex. QLAB Software was used to obtain quantitative analysis of renal perfusion including:
□ the slope rate of ascending curve (A),
□ the time to peak (TTP),
□ the derived peak intensity (DPI),
□ the area under the curve (AUC).

Results: Our retrospective study involved 381 patients (391 grafts of which 71 DGF and 10 PNF); the univariate analysis of the results revealed that there was a statistically significant difference between upper and lower RRI and their average in patients with DGF and patients with Early Graft Function (EGF) p Value 0.0001. No correlation between RRIs and PNF was found. Our prospective study included 25 patients; 7 of them developed a DGF. The results revealed that TTP in patients with DGF seems to be reached later than in patients with EGF. AUC was lower in the DGF group. No correlation between A and DPI and functional recovery of the graft was found. Statistical Analysis of these values, although, isn’t available yet.

Conclusions: The well-known usefulness of the color-doppler ultrasound study in the transplanted kidney is confirmed, adding to its characteristics the possibility of use as a tool to predict grafts outcome. Further studies are needed to determine CEUS capability in the prediction of grafts functional recovery and to obtain a Perfusion Index, which will be the milestone of a new predictive model based on visual and numerical feedback.

332.10
Pre-transplant Coronary Angiography Findings Based on Coronary or Aorto-Iliac Calcification on CT Imaging in Asymptomatic Patients With a Negative Cardiac Stress Test

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Purpose: Cardiac events are now the leading cause of early mortality after kidney transplantation. Long term exposure to immunosuppression also increases cardiometabolic stress after transplantation. Several studies in general population have shown that the presence of coronary artery calcification increases the risk of future cardiovascular events. Among pre-kidney transplant candidates, there remains wide variation in cardiac risk assessment practices across transplant centers. We report coronary angiography findings in asymptomatic candidates undergoing Kidney transplant evaluation with negative stress test but with findings of coronary or aorto-iliac calcification on CT imaging.

Methods: We conducted a retrospective single center study of 76 Pre-Kidney transplant recipients who had a negative stress test and underwent coronary angiography between 2010 to 2021. All patients underwent coronary angiography based on coronary or aortoiliac calcification on CT imaging. Mean age was 60 years in both groups. Demographics and results are listed in table 1.

Results: Results at our academic center showed that 18 out of 76 patients (23.6%) had a 70% stenosis in one or more coronary vessels. 11 out of 76 patients (14.4%) underwent single or multiple vessels stent placement and one underwent CABG. 7 out of 76 patients (9%) had significant distal disease or vessels were too small for intervention. In CAD group, 13 out of 18 patients (72%) were diabetic. All patients underwent successful kidney transplantation. Post Operative hypotension was more common in non-CAD group, in 9 patients as compared to 3 patients in CAD group. 5 patients in non-CAD group had post-op Atrial fibrillation Vs 1 in CAD group.

Conclusions: In addition to traditional risk factors and other cardiac risk stratification modalities, Coronary or aorto-iliac calcification on CT imaging is a predictor of significant coronary artery disease in patients undergoing evaluation for kidney transplant surgery. coronary angiography before transplantation should be considered for potential candidates for Kidney transplant with negative stress test but significant vascular calcification.
Test Performance of 2-Stage Screening of BKV Infection With Urine Cytology and Serum Quantitative Polymerase Chain Reaction: A Prospective Study


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Introduction: Early detection of BK virus replication and prompt reduction of immunosuppressant at earlier stage of disease is the key of success in management of BKVAN. Our group had demonstrated BK virus screening with urine cytology and BKV serum quantitative polymerase chain reaction (qPCR) is a cost saving method to identify early infection. However, prospective data on the test performance of 2-stage screening is lacking.

Materials and Methods: Kidney transplant recipients within first 5 years post-transplant and those with graft dysfunction (including after anti-rejection therapy) were included. Recruited patients had regular urine cytology: every 3 months from the time of transplantation until the end of the first year post-transplantation and then annually till 5-year post-transplant. Additional urine cytology tests were performed in patients after anti-rejection therapy. Quantification of serum BK viral load by qPCR was performed in patient who had urinary decoy cell. BK virus associated nephropathy (BKVAN) was defined as sustained plasma BKV DNA and loads of >4 log10 cp/mL with or without biopsy proven BKVAN.

Results: 509 patients were recruited (1740 patient-years) and were followed up for 3.2 years in average. 33 patients were diagnosed to have BKVAN and increasing viraemia after graft biopsy. The negative predictive value of 2-stage screening was 98.1%.

Conclusions: The incident of BKVAN is low in Hong Kong and kidney transplantation within first two years has higher risk of BKVAN. Routine BK virus screening with urine cytology and BKV qPCR has low false negative rate and would be the screening protocol of choice in places who cannot afford the high cost of routine BKV with qPCR. Extending the every 3 months screening period to up to 2-year post-transplant may help to improve the performance of this screening protocol.

Association Between CYP3A5*1 and CYP3A5*3 Polymorphisms, With the Formation of ADES and the Presence of Rejection in Renal Transplant Recipients

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Background: Tacrolimus is metabolized by the CYP3A5 pathway, of which different genomic variants have been described: CYP3A5*3/3 “non expresser” do not express functional protein, but not: CYP3A4*1/1 AND CYP3A5*/3 They are functional genotypes. A risk factor for presenting specific anti-donor antibodies, as well as rejection episodes, is the variability in serum levels of tacrolimus. Variability can be expressed as: Standard deviation, (SD) Coefficient of variability, or (CV) Time in therapeutic range, (TTR).

Objectives: To find the association or not between the CYP3A5 polymorphisms studied with the formation of ADES de Novo and the presence of rejection.

Material and methods: Kidney transplant recipient patients from January 1, 2010 to January 1, 2020. Take variability with different measurements of tacrolimus, according to the different types of CYP3A5*1 and CYP3A5*3 polymorphisms. Study time: 3,6,12 months post transplant, and with different variability index.

Results: Student’s T analysis of independent variables was performed, reporting an O.R. of 3.5, with a 95% confidence interval of (-12.29 – 19.37), with a p value of 0.653, the association not being significant. No significant association was found in the univariate analysis between greater variability of serum tacrolimus, allelic status, with the development of de novo ADES and renal graft rejection. Statistical significance was found between the CYP3A5 variant and the intrapatient tacrolimus serum variability coefficient percentage.

Discussion: Previous studies have reported a significant association, between greater intrapatient serum tacrolimus variability, with the development of de novo ADES, as well as with a higher incidence of renal graft rejection. A significant association was found between the CYP3A5 variant and the intrapatient tacrolimus serum variability coefficient percentage.

Conclusion: In the present study, no significant association was found in the univariate analysis between greater variability of serum tacrolimus, allelic status, with the development of de novo ADES and renal graft rejection. Statistical significance was found between the CYP3A5 variant and the intrapatient tacrolimus serum variability coefficient percentage, which, together with a longer follow-up time, could, associated with other previously mentioned risk factors, manifest as rejection events, kidney graft and development of de novo ADES, when presenting a subtherapeutic level of tacrolimus, for longer periods of time.
Young Adults With Liver Transplantation: An Analysis of the Information Registry and Management System of Argentina (SINTRA)

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Introduction: The pediatric population of Argentina, especially those under 12 years old, access to liver transplantation through the MELD score exception. This fact might cause inequities since young adult's recipients are at high risk factor for worse graft survival after liver transplantation. In this study we evaluated liver transplantation waitlist and post-transplant outcomes in those aged 18 to 24 years compared to younger waitlist registrants and recipients.

Method: we performed a multivariate logistic regression to examine the association between age at listing (0-5, 6-11,12-17 and 18 -24 years [the reference category]) and waitlist outcomes: drop out and transplantation. The model included the following features: emergency category, whether an exception score was granted, serum albumin, ABO blood group, and insurance payer status. The database used was the Information Registry and Management System of Argentina (SINTRA). Graft and patient survival were stratified by these age categories using Kaplan Meier curves to perform the analysis of transplant outcomes.

Results: between 2006 and 2020, 1842 on first time transplants registrants and 794 recipients were included. Registrants aged 0 to 17 were less likely to experience dropout from the waitlist compared with those aged 18 to 24 years (adjusted hazard ratio, 0-5: OR 0.21 (0.16-0.30); 6-11: OR 0.36 (0.22-0.59); 12-17: 0.57 (0.39-0.86); 18-24: 1.00), and better transplant survival analysis, recipients aged 18 to 24 years had a similar risk of graft failure and death compared with all other groups.

Conclusion: This study showed that there was not differences in liver graft failure and death between young adults ages 18 to 24 years and children. However, younger age liver transplant patients had had higher probability of drop out from the waitlist and less probability of being transplanted compared to younger age groups.

Vascular Complications in Pediatric Liver Transplants And Their Management

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Introduction: Unlike other organs, the blood supply of the liver occurs through two systems. One of these is the hepatic artery, and it supply approximately one-third to one-fifth of the liver. The rest of the liver is supplied with blood via the portal vein. The outflow of blood circulation in the liver is via the hepatic veins. Any disruption in this blood circulation results in deterioration in liver functions. In this study, we aimed to evaluate early vascular complications in pediatric liver transplants.

Methods: From 8 November 1988 to 31 December 2021, we performed 701 LT procedures and 334 of them were pediatric.). We reviewed the medical records of these recipients for the following: primary cause of liver failure, age, and weight at the time of transplantation, type of graft, vascular complications and their management. One hundred and seventy six of the recipients were male and 158 were female. Mean age of 7.34 years (0.5 months – 17 years). Nineteen (5.7%) of the LT were deceased donor LT and 315 (94.3%) were living related liver transplant. Most cause of liver failure was biliary atresia (n=169). Mean weight of recipients was 23.5kg. Most of graft types was left lateral graft (n=204)

Results: Hepatic vein complications occurred in 3 patients. In all three patients, stenosis was detected in the portal vein anastomosis region and was successfully treated with interventional radiological methods by placing a stent in the anastomosis region. Portal vein complications occurred in 3 patients. In one of these patients, hemostasis was performed by surgical method due to bleeding from the portal vein anastomosis. In the second patient, the anastomosis was surgically revised due to thrombus formation in the portal vein. In the third patient, due to a stenosis of more than 50% in the portal vein anastomosis, a stent was placed in the anastomosis region after balloon dilation using interventional radiological methods, and blood flow was successfully maintained. Hepatic artery complications occurred in 54 patients. Hepatic artery thrombosis occurred in 31 patients, hepatic artery stenosis in 13 patients, bleeding from hepatic artery anastomosis in 7 patients, hepatic artery dissection in 2 patients, and pseudoaneurysm in the hepatic artery in 1 patient. 43 of these patients were successfully treated with interventional radiological methods and 11 of them surgically.

Conclusion: Vascular complications seen in liver transplants can cause deterioration in hepatic functions and acute liver failure. Especially hepatic artery complications are one of the most important causes of biliary tract complications that will develop in the future. Vascular complications can be successfully treated at an early stage in experienced organ transplant centers.
Impact of Previous Abdominal Surgery on Laparoscopic Donor Hepatectomy for Living Donor Liver Transplantation

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Introduction: Laparoscopic donor heptatectomy (LDH) has many advantages over open donor heptatectomy. However, previous abdominal surgical history can be considered to cause difficulties in laparoscopic surgery. Few studies have evaluated the impact of previous abdominal surgery (PAS) on LDH. Therefore, we studied the effect of PAS on LDH.

Method: This study is a retrospective study conducted at a single center. We reviewed the data of 361 patients who underwent LDH at Samsung Medical Center from January 2017 to December 2020. These patients divided into 72 patients with previous abdominal surgery (PAS) group and 289 patients with non-previous abdominal surgery (non-PAS) group. Two groups were compared with respect to operation factors such as estimated blood loss, operation time, and intraoperative blood transfusion. Postoperative outcomes such as length of hospital stay, postoperative complications, AST, ALT, INR, albumin, and total bilirubin trends (preoperative, peak-postoperative and 1 month). All donors fully recovered and returned to their normal activities.

Result: 72 patients have previous abdominal surgical history [cholecystectomy (4), splenectomy (1), pyeloromyotomy (1), cesarean section (28), appendectomy (19), uterine surgery (8), ovarian surgery (7), hernia repair (3), laparoscopic anterior resection (1)]. There was no statistical difference in estimated blood loss and operation time between the two groups. No donors received intraoperative blood transfusion. Complications occurred in 7 patients (9.7%) in the PAS group and in 26 patients (9%) in the non-PAS group, and there was no statistical difference between the two groups. There were no significant differences in the changes in AST, ALT, INR, albumin, and total bilirubin (preoperative, postoperative and 1 month). All donors fully recovered and returned to their normal activities.

Conclusion: The outcomes of our study show the feasibility and safety of LDH in patients with previous abdominal surgical history. Therefore, even if there is a history of PAS, LDH can be performed safely enough, so it is not a contraindication.

An Analysis of Deceased Donor Liver Offers to Adolescent Compared to Young Adult Liver Transplant Candidates

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Introduction: Minimizing waitlist mortality among pediatric liver transplant candidates is a priority. Yet, organ acceptance practices are variable, and half of the children who die on the waitlist receive at least one liver offer that is declined. It is unclear if the willingness to accept liver offers differs between adolescent and young adult candidates. We studied deceased donor liver offer acceptance in adolescent vs. young adult liver transplant candidates, hypothesizing that adolescents would have lower acceptance rates than young adults.

Methods: This was a retrospective cohort study using the SRTR registry and potential transplant recipient file to identify deceased donor liver offers to liver transplant candidates aged 11-26 between 2009-2019. We excluded the following offers: those refused due to size, offers to candidates outside of the first 40 positions on the waiting list, and offers for livers that were ultimately discarded. We additionally stratified the analysis by quality of offered liver, defining lower quality as donation after circulatory death donors, steatotic livers (>30% macrosteatosis), or donors >40 years old. Our exposure was candidate age: adolescent (11-17yo) vs. young adult (18-26yo). The outcomes compared across age groups included: number of offers received, liver offer acceptance, transplant rate, waitlist mortality, and removal for being too sick. We compared these offer metrics for higher vs. lower quality donor liver offers. Offer acceptance rate was adjusted for MELD/PELD at listing, donor age, and donor/candidate size.

Results: We studied 15,628 liver offers (50% higher quality) to 4,901 waitlisted candidates (37% age 11-17, 63% 18-26). The table shows offer metrics by age group. Compared to young adults, adolescents were more likely to be transplanted (65.4% vs. 56.5%, P<0.001) and less likely to die (4.4% vs. 7.9%, P<0.001) or be removed from the waitlist (3.0% vs. 6.3%, P<0.001). Adolescent recipients were less likely than young adults to receive a lower quality liver (11.2% vs. 35.5% of recipients, P<0.001). The overall acceptance rate for higher quality liver offers was 28.3%. Adolescents received more high-quality offers (3.0 vs. 2.4, P<0.001) and had slightly higher acceptance of these offers (29.7% vs. 26.9%, P=0.032) compared to young adults. For lower quality offers, adolescents received fewer offers (1.2 vs. 2.2, P<0.001) and had a similarly low acceptance rate (8.5 vs. 10.3%, P=0.061).

Conclusion: Seven out of ten transplantable deceased donor liver offers received by pediatric and young adult candidates are declined on their behalf. Offer acceptance rates for high quality livers are similarly low for adolescents and young adults. Efforts to increase offer acceptance rates, taking care to safeguard post-transplant outcomes, may improve access to pediatric liver transplantation.

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Osteopenia Predicts Posttransplant Survival Among Livingdonor Liver Transplant Recipients

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Introduction: Osteopenia, loss of bone mineral density (BMD), was recently identified to be independently associated with early mortality as the risk factor for mortality after living-donor liver transplantation (LDLT) compared with already-reports predictors in a large cohort of Japanese patients with liver cirrhosis. The aim of this study was to clarify the impact of osteopenia as the risk factor for mortality after living-donor liver transplantation (LDLT) compared with already-reported predictors in a large cohort of Japanese patients with liver cirrhosis.

Methods: Data were collected retrospectively for all consecutive 609 patients who underwent LDLT at our institution between January 2001 and November 2019. BMD was evaluated with computed tomographic measurement of pixel density in the midvertebral core of the 11th thoracic vertebra by computed tomography. Data related to clinicopathological parameters and diagnosis were analyzed by dividing into two groups; acute liver failure groups (n=62) and decompensated liver cirrhosis (n=547).

Results: (1) Acute liver failure groups (n=62): The median value of BMD was 210.4 Hounsfield units (HU). Osteopenia was identified in 18 (29.0%) of 62 recipients, according to the calculated age-specific standard BMD values. The overall survival of the patients of osteopenia was similar to that of patients with non-osteopenia (P-value=0.052; 5y, 55.6% vs. 76.8%). (2) Decompensated liver cirrhosis groups (n=547): The median value of BMD was 171.6 Hounsfield units (HU). Osteopenia was identified in 251 (45.9%) of 547 recipients. The overall survival of the patients with osteopenia was significantly lower than the patients with non-osteopenia (P-value<0.001; 5y, 71.5% vs. 89.7%). In addition to the other predictors, such as preoperative high PELD score (<30 vs ≥30) (p 0.006), preoperative low body weight (<6 vs ≥6 kg) (p 0.025) and presence of postoperative hepatic artery complication (p 0.024), osteopenia was independent risk factors for mortality after LDLT by multivariate analysis.

Conclusion: Preoperative osteopenia was independently associated with post-LDLT mortality among patients with decompensated liver cirrhosis. Improving osteopenia with preoperative rehabilitation or medical therapy may improve post-LDLT survival.

Predisposing Risk Factors in Liver Transplants Younger Than 3 Years

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Aim: Liver transplant (LT) is the standard treatment for pediatric end stage liver disease. One year graft and survival rates after pediatric LT are reported to be near 90%. However, complications often persist and can adversely affect outcomes, so early detection is essential, especially for smaller pediatric patients. We, here, aimed to evaluate the predisposing risk factors affecting the early LT outcomes in children ≤3 years old, as can be named as the most challenging group of the liver transplant.

Materials and Methods: Since December 1988, we performed 701 liver transplant (LT) procedures (334 pediatric, 367 adult) at our center. Among these 334 pediatric liver transplants, 146 patients were younger than 3 years old (mean 14, 94 months). We retrospectively evaluated the demographic and surgical features of these patients younger than 3 years old and define the predisposing factors affecting the early LT outcomes.

Results: Among these 146 recipients who were ≤3 years, we lost 14 LT patients during the first month of LT. Besides these early mortality 61 LT survived for 2-10 years, 41 LT survived for more than 10 years. The retrospective analysis of the patients were done according to the demographic data, surgical features and postoperative complications. Our overall patient and graft survival rates and the risk factors were found to be similar with the previous reports. The results showed that predictors of early mortality were found to be; preoperative high PELD score (<30 vs ≥30) (p 0.006), preoperative low body weight (<6 vs ≥6 kg) (p 0.025) and presence of postoperative hepatic artery complication (p 0.024).

Conclusion: Greater caution is needed for pediatric patients with low body weight and high PELD scores and further technical innovations and careful management are required to deal with hepatic artery reconstruction to improve survival of LT patient’s ≤3 years old.
333.7
Measurement of Quality of Life in Adolescent Transplanted Patients: A Necessary Approach

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Introduction: Liver transplantation is the option for pediatric patients with acute or chronic terminal diseases. Multiple innovations have been made to transplant programs worldwide to improve effectiveness, safety and timely services. Until now, only hard indicators (survival/complication rate) have been used to evaluate effectiveness of transplantation. Since these indicators are not enough, it is necessary to include the perspective of the patient and their family to determine the impact that the transplant has on their quality of life. Even though there is no “gold standard” to measure the health related quality of life (HRQoL) in our center, the use of generic HRQoL questionnaires allows an objective evaluation of their quality of life. The objective of the present study is to analyze and describe the results of the PedsQL 4.0 Generic Questionnaire when applied to adolescent patients who received a liver transplant in a public hospital in Argentina, and compare them to healthy adolescents.

Methods: PedsQL 4.0 Generic Core Scale was applied to 45 adolescent (older than 17 years old) who had received a liver transplant more than 10 years ago. The scale is a self-reported 5-point Likert scale with 23 items that ranges from 0 (Never) to 4 (Almost always). It is brief and multidimensional, as it includes Physical, Emotional, Social, and School Functioning dimensions. Results were linearly transformed to a 0-100 scale (0=100, 1=75, 2=50, 3=25, 4=0). Total score (as well as Psychosocial Health Summary Score and Physical Health Summary Score) was calculated as mean and SD. T-test was used to compare with data extracted from the literature from previous validation studies for Argentinian healthy adolescents.

Results: A total of 45 patients completed the survey. Missing items were only 0.7% of items, so complete data for all patients was included. No difficulties with the format nor the form of administration of the questionnaire were found. 51% of patients were female, with a median follow-up of 15.52 years. PedsQL Total Score was 73.89 (15.01) vs 72.72 (14.21) in healthy adolescents, and showed no statistical difference among them (p=0.84). The Psychosocial Health Summary Score was 69.96 (16.59) vs 71.20 (14.84), while the Physical Health Summary Score was 81.25 (15.55) vs 75.42 (15.93) in healthy patients respectively (p=0.846 and 0.334).

Conclusions: In this study, no difference in HRQoL was found among adolescents transplanted patients when compared with published data from healthy population. Even though this is an initial approach to measuring quality of life and some limitations could be found (small sample size, generic module and literature comparison), further studies are needed to validate specific questionnaires for transplanted patients in our center, focusing on the unique aspects of this chronic condition. We consider this measure a necessary endpoint of the transplant in order to complete and improve patient’s care and results.

333.9
The Effect of Short-term Inhalation of Isoflurane on the Outcomes of Intraportal Hepatocyte Transplantation

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Introduction: Liver transplantation is currently established as a treatment for endo-stage liver disease. However, this treatment is considered too invasive for those patients. Hepatocyte transplantation (HTx), which is less invasive in comparison to liver transplantation, has been expected to serve as an alternative therapy to liver transplantation. However, the outcomes of HTx are still far from satisfactory, and it is well known that there is a large discrepancy between the experimental results of animal models and clinical outcomes of HTx. Of particular note, clinical HTx is only performed without general anesthesia, while inhalation anesthetics are usually used in animal experiments. Isoflurane, which is one of the most widely used inhalation anesthetics in animal experiments, is known to have a strong vasodilatory effect, portal pressure inhibitory effect, and cytoprotective effect against cytokine-induced injury. Therefore, we hypothesized that isoflurane may be a possible reason for the discrepancy between the results of animal experiments and the clinical outcomes of HTx.

Methods: F344/NStLc rat hepatocytes were isolated. Isolated hepatocytes (1.0×10^7 cells) were transplanted to anabuminemic rats with (ISO group) and without (AW group) isoflurane. These anabuminemic rats had a syngeneic background to the donor rats. The serum albumin, AST, ALT, LDH levels and several inflammatory mediators in the recipient rats were analyzed. Immunohistochemical staining and ex vivo imaging of transplanted hepatocytes were also performed.

Results: The serum albumin levels of the ISO group were significantly higher in comparison to the AW group (p<0.05) (Figure 1). The serum AST, ALT, LDH levels of the ISO group were significantly suppressed in comparison to the AW group (p<0.0001, respectively). The serum levels of IL-1β(p<0.01), IL-10 (p<0.01), IL-18 (p<0.01), MCP-1 (p<0.05), RANTES (p<0.01), Fractalkine (p<0.01), and LIX (p<0.05) in the ISO group were significantly downregulated in comparison to the AW group. The ischemic regions of the recipient livers, which were easily detected in the livers of both groups, tended to be more evident in the AW group (3.69±1.05%) in comparison to the ISO group (2.42±1.76%) (Figure 2).

Conclusions: This study showed that the anti-inflammatory effects of isoflurane could efficiently contribute to hepatocyte engraftment. According to the detailed analyses in this study, the anti-inflammatory effects, rather than vasodilatory effects, of isoflurane appeared to be the main mechanism of the abovementioned benefits. Isoflurane may at least in part be a reason for the discrepancy between the results of animal experiments and the clinical outcomes of HTx.
The Role of Immunosuppression Level in Liver Allograft Fibrosis After Pediatric Liver Transplantation

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Objective: Liver allograft fibrosis (LAF) is prevalent among patients with long-term survival after liver transplantation (LT). We aimed to identify clinical risk factors associated with LAF in pediatric LT recipients, with a focus on the impact of immunosuppression level on LAF and its evolution.

Methods: A retrospective study on pediatric LT recipients with at least one-year follow-up who underwent liver biopsy was conducted. Cox regression models were used to analyze risk factors associated with LAF, and landmark analysis was used to evaluate the impact of tacrolimus (TAC) level on LAF. Longitudinal analysis was also conducted in patients undergoing repeat liver biopsies.

Results: A total of 139 patients involving 174 liver biopsies were included. With a 2.3-year follow-up period, LAF was detected in 91.4% of patients (9.4% had severe LAF). Episodes of acute rejection, biliary complications, positive cytomegalovirus DNA after LT, and prolonged cold ischemia time were independent risk factors for LAF.

The risk in the low TAC level group at 1-3, 3-6, 6-12 and 12-36 months after LT was higher than the counterparts. Especially, in patients with high TAC level (≥ 5.1 ng/mL) during postoperative 1-3 years, the risk of LAF was 67% lower in the short-term (P = 0.006). Twenty-six patients underwent repeat liver biopsies. Patients with increasing TAC level after the first biopsy were more likely to achieve fibrosis reduction (HR = 7.53, P = 0.025).

Conclusion: LAF is common among pediatric LT recipients with more than one-year of follow-up, but was mostly mild or moderate. Under-immunosuppression may contribute to the development of fibrosis; and the degree of LAF may be improved by administering adequate levels of immunosuppression.
Sequential Abdominal Closure After Pediatric Lateral Left Side Segment Hepatic Transplantation

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Introduction: After pediatric left lateral segment (LLS) liver transplantation for small children, primary abdominal wall closure may not be possible or not recommended. Reduction of the graft, using a monosegment graft or deferred wall abdominal closure are possible alternatives. We describe our results with sequential abdominal closure (SAC) with polytetra-fluoroethylene mesh in pediatric LLS recipients.

Method: Retrospective review of patients who received LLS and CAS with polytetra-fluoroethylene mesh between 2010 and 2021. The mesh was placed and fixed with continuous polypropylene suture to the wall on both sides of the incision. Mesh flap approaches were performed in the PICU under sedation, with ultrasound control before and after, without requiring intubation. The mesh was removed in the operating room under general anesthesia after complete approximation of the flaps. The data were recorded from the patients’ medical records after approval by the ethics committee.

Results: Of 198 who received an LLS, 86 (43.4%) required a SAC. Mean age was 2±3.1 years and mean weight 9.2±5.4 Kg. LLS was obtained from living donors (54.6%) and split (45.4%) with a mean graft weight of 324.1 grams. The graft weight/recipient weight ratio was 3.9±1.4%. The mesh was removed after 8.2±3.4 days, requiring 3.2±1.6 sequential approaches per patient. Six surgical wound infections and five wound dehiscence during the process were recorded. No systemic infection related to the mesh or compartment syndrome occurred. The mesh was directly removed in 81.4%, while 18.6% were reoperated for complications (vascular, biliary or intestinal) prior to its removal. After definitive closure, one (1.2%) patient had partial dehiscence and six (7%) suffered surgical wound infections. No grafts were lost due to sac procedure-related causes. The median follow-up time was 53 (15-84.3) months.

Conclusion: SAC with polytetra-fluoroethylene mesh offers a reproducible and safe solution for difficult or not advisable abdominal closure after pediatric liver transplantation of LLS. The presence of the mesh during the immediate postoperative period represents an advantage for the review of the graft status and possible complications in the immediate postoperative period. Hyper-reduction of the graft or the use of a monosegment could be avoided in most cases.
Up-Regulated LRRN2 Expression as a Marker for Graft Quality in Living Donor Liver

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Introduction: The quality and size of liver grafts are critical factors that influence living donor liver transplantation (LDLT) function and safety. However, the biomarkers used for predicting graft quality are lacking. Only donor age has been used as a graft quality marker, and the mechanism of increased donor age and decreased graft function is not well understood. In rodents, several functional and genetic changes reportedly occur in the liver with aging. However, there are some problems that short-lived rodents cannot adequately reproduce human aging. Non-human primates are considered one of the best preclinical models due to their genetic, physiological, and anatomical similarities to humans compared to rodents. In this study, we sought to identify unique graft quality markers, aside from donor age, by utilizing the livers of non-human primates.

Methods: Hepatic gene microarray analysis from young (n=7, 5-9 years old) and elderly (n=6, 26-27 years old) cynomolgus macaques was performed to examine the age-related gene change. The candidate age-related gene expression in 350 human LDLT donor liver tissue was examined by rtPCR. The correlation between the gene expression and 6-month graft survival rates was investigated.

Results: We conducted the principal component analysis with microarray analysis data and observed clear segregation of young and elderly groups, suggesting the age-related changes in gene expression were obviously captured. In addition, this analysis revealed a total of 271 genes with significantly increased expression in the elderly. These candidate genes were then narrowed down to six through bioinformatics analyses. The expression patterns of these candidate genes in human donor liver tissues were subsequently examined. Importantly, we found that grafts exhibiting up-regulated expression of these six candidate genes were associated with an increased incidence of liver graft failure. Multivariate analysis further revealed that up-regulated expression of LRRN2 (encoding leucine-rich repeat protein, neuronal 2) in donor liver tissue served as an independent risk factor for graft failure (Odds ratio 4.50, confidence interval 2.08-9.72, p-value = 0.0003). Stratification based on graft expression of LRRN2 and donor age was also significantly associated with 6-month graft survival rates [LRRN2 low/donor age < 50 years; 97.3% LRRN2 low/donor age ≥ 50 years; 100%, LRRN2 high/donor age < 50 years; 95.1%and LRRN2 high/donor age ≥ 50 years; 66.6%, p-value < 0.0001].

Conclusions: Uregulated LRRN2 expression of liver graft is significantly correlated with graft failure in LDLT. In addition, the combination of graft LRRN2 expression and donor age may represent a promising marker for predicting LDLT graft quality.
A Gelatin Hydrogel Nonwoven Fabric Improves Outcomes of Subcutaneous Islet Transplantation

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Introduction: Subcutaneous islet transplantation is a promising treatment for severe diabetes, since it has several advantages, including minimal invasiveness and easy accessibility for the islet grafts, which makes it possible to monitor and/or remove islet grafts if needed. However, poor vascularization has long been regarded as major drawback in this transplant site. Recently, several groups have reported that the compensation of extracellular matrix (ECM) is also crucial for successful subcutaneous transplantation. We previously reported that a recombinant peptide (RCP) enhances subcutaneous islet engraftment. However, it is impractical for clinical use because RCP must be removed when transplanting islets. We herein investigated whether a novel bioabsorbable gelatin hydrogel nonwoven fabric (GHNF) could improve subcutaneous islet engraftment.

Methods: A silicon spacer with or without GHNF was implanted into the subcutaneous space of diabetic mice at 6 weeks before islet transplantation. Syngeneic islets (400 islet equivalents) were transplanted into the pretreated space or intraportally (Ipo group). Blood glucose, intraperitoneal glucose tolerance, immunohistochemistry, CT angiography and gene expression were evaluated.

Results: The cure rate (Figure 1) and glucose tolerance of the GHNF group were significantly better than in the control and Ipo groups (p<0.01, p<0.05, respectively). In the GHNF group, a limited increase of vWF-positive vessels was detected in the islet capsule, whereas laminin (p<0.05), collagen III and IV were considerably enhanced. CT angiography revealed that the blood vessel volume surrounding the silicon spacer was comparable between the GHNF and control groups. TaqMan arrays revealed a significant upregulation of 19 target genes (including insulin-like growth factor-2 (IGF-2)) in the pretreated space (p<0.05) (Figure 2). The protein level of IGF-2 in the supernatant of the homogenized subcutaneous fibrous capsules in the GHNF group was also significantly higher than that in the control group.

Conclusions: Pre-implantation of a GHNF effectively improved subcutaneous islet engraftment, resulting in much better outcomes in comparison to intraportal islet transplantation. This beneficial effect may be mainly due to the compensation of ECM for the islet capsule and protection of islet viability by various growth factors, rather than the enhancement of neovascularization.

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Presentation of FasL Protein by PEG Microgels Within Graft Site Leads to Survival of Pancreatic Islets in Nonhuman Primates Without the Need for Chronic Immunosuppression

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Introduction: Allogeneic islet transplantation is a viable clinical approach to treat type 1 diabetes. The need for chronic immunosuppression to control rejection is a major impediment for the broad application of allogeneic islet transplantation. T effector cells responding to alloantigens initiate and coordinate graft rejection. These cells upregulate Fas receptor following activation and become sensitive to Fas-mediated apoptosis. In a rodent model, we previously reported the efficacy of PEG microgels engineered to display a novel form of FasL (SA-FasL) on the surface in inducing localized tolerance to allogeneic islets. We herein report the efficacy of this immunomodulatory regimen in preventing rejection of allogeneic islets in a NHP model in the absence of chronic use of immunosuppression.

Methods: PEG microgels formulated with biotin were engineered to display SA-FasL protein on the surface. Engineered microgels were co-transplanted at 2:1 ratio with islets (PEG/islet) into the omentum of STZ-diabetic allogeneic cynomolgus recipients. Un-engineered microgels without SA-FasL co-transplanted with islets served as controls. Recipients were kept on a 3-month rapamycin regimen as the only maintenance therapy. Animals were monitored for graft survival up to 6 months and subjected to IVGTT and surgical removal of the graft to assess function.

Results: Immunomodulation with PEG presenting SA-FasL resulted in graft survival in all recipients (n=4) for ~180-day experimental end-point. In marked contrast, all control recipients (n=3) under the same rapamycin regimen rejected the graft in an acute fashion. Graft recipients promptly achieved excellent glycemic control with normal fasting blood glucose levels. Intravenous glucose tolerance test performed at 3- and 6-month post-transplantation revealed excellent islet function, comparable to naïve animals. Importantly, surgical removal of the transplant resulted in prompt hyperglycemia, demonstrating graft function, which was further confirmed by fasting and stimulated insulin and c-peptide levels. Graft survival was associated with increased number of FoxP3+ T regulatory cells in the graft site with no significant changes in the systemic frequency of various T cell subsets. Furthermore, T cells from long-term graft recipients responded to donor antigens at comparable levels to pre-transplant T cells, indicating the localized nature of induced tolerance. This immunomodulatory protocol did not result in significant alterations in the liver and kidney metabolic function, demonstrating safety.

Conclusions: Immunomodulation with PEG microgels presenting SA-FasL is effective in overcoming rejection of allogeneic islet grafts in NHPs in the absence of chronic immunosuppression. Thus, PEG microgels presenting SA-FasL, as an off-the-shelf product has considerable clinical potential for the treatment of type 1 diabetes.

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Evidence for Xenogeneic Hematopoiesis After Peripheral Blood Stem Cell Transplantation From a Novel Transgenic Pig With Knock-in hIL-3 Receptor

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Introduction: Xenotransplantation poses a heightened immunologic barrier; therefore, tolerance induction strategies are needed. Mixed chimerism (MC) has successfully induced tolerance in xenogeneic humanized mouse models. In these models, porcine hematopoietic cytokines are needed to support porcine MC. Our study uses a transgenic pig with a humanized IL-3 receptor (Tg hIL-3R) in addition to hCD47 to support engraftment of mobilized porcine peripheral blood stem cells (PBSC) to promote MC in a pig-to-baboon model.

Methods: A novel GalTKO/hCD46/hCD47/hCD55/hCD59 Tg, hCD123/hCD131/hCD116 knock-in pig underwent mobilization with porcine stem cell factor (p-SCF) and porcine IL-3 prior to leukapheresis. PBSC product, dosed at 1x10^9 mononucleated cells/kg, was infused into two P. hamadryas baboons on days 0, 49 and 63 after non-myeloablative conditioning with total body and thymic irradiation, rituximab, ATGAM, LoCD2b and anti-CD154. Tacrolimus and pSCF was given from day 0 to 28. Two control baboons received the same protocol, without PBSC. Donor skin from the donor pig was grafted at week 12 to test tolerance. Controls will be grafted this month. Grafts were serially monitored using punch biopsy and photography.

Results: Mobilized porcine PBSC expressed the hGM-CSF and hIL-3R alpha chains, but only the hIL-3R was functional in vitro. Peripheral blood chimerism (PC) was elevated in the first 48-hours compared to current and historical controls that received PBSC from pigs not Tg for hIL-3R. The experimental animals demonstrated a relative increase in PC at day 15-23 compared to all controls. Xeno-antibody levels were reduced from pre-transplant levels until skin grafts rejected, while control animals maintained stable levels during the initial 30 days. Donor skin grafts survived 37 and 41 days, similar to historical MC controls receiving PBSC and skin from GalTKO hCD47hi pigs. After grafts were rejected, the two animals were euthanized and the bone marrow (BM), thymus, liver and lymph nodes were examined for potential engraftment. Porcine lymphocytes were found only in the liver and represented >20% of total live leukocytes for both baboons. These cells were further characterized to be CD3⁺CD4⁻ gamma delta T cells.

Conclusion: Due to the remarkable percentage of porcine gamma delta T cells found in the liver at 173 post-infusion, we hypothesize that the liver is an immunoprivileged site for xenogeneic T cells, allowing for cell survival. We continue to explore the infusion of xenogeneic stem cells into protected compartments, such as intra-bone BM transplant, to support porcine stem cell survival. The increase in PC at days 15-23 demonstrates evidence for later stage hematopoiesis in these animals, which has not previously been seen in our studies. This can be attributed to the functional Tg hIL-3R, supporting the hypothesis that genetic engineering of cytokine receptors provides a strategy to enable prolonged MC to promote xenogeneic tolerance.

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Porcine SLA-Specific Car Treg Enable Xenotransplantation in the Absence of Immunosuppression

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Introduction: Recent successes in xenogeneic organ transplantation in humans raise hopes of overcoming the worldwide organ shortage. The availability of cells, tissues, but also solid organs of porcine origin could counteract this critical circumstance from a medical point of view and reduce the increasing gap between available donor organs and patients with end-stage organ dysfunction by xenotransplantation. In contrast, the immunological barrier must be overcome. With the development of new immunosuppressants and the generation of less immunogenic donor animals, this barrier can be reduced. However, it is unclear whether this approach will lead to long-term acceptance.

Methods: Here, we describe the generation of a specific chimeric antigen receptor (CAR) that recognizes the porcine SLA*0401 molecule.

Results: Modification of natural Tregs (nTregs) with the SLA CAR alters the specificity of polyspecific Tregs for antigen-specific regulators without affecting their phenotype, stability, or epigenetics. Compared to nTregs, SLA CAR-Tregs showed significantly better ability to control strong immune responses in vitro and in vivo. In the humanized mouse model (NRG mice), the use of SLA CAR-Tregs resulted in the prevention of xenogeneic target cell rejection. In the highly immunogenic skin transplantation model, adoptive SLA CAR-Treg transfer protected porcine skin from recipient-driven immune responses. In the streptozotocin-induced diabetes model in NRG mice, porcine islet cells transplanted under the kidney capsule were able to restore normoglycemia after SLA CAR-Treg transfer.

Conclusion: These modified CAR-Tregs have great potential for inclusion in xenogeneic organ transplantation protocols in humans, extending graft longevity through their potent immunoregulation.

Xenotransplantation of Genetically Modified Neonatal Pig Islets Cures Diabetes in Baboons

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Xenotransplantation using porcine donors is rapidly approaching clinical applicability as an alternative therapy for treatment of many end-stage diseases including type 1 diabetes. Porcine neonatal islet cell clusters (NICC) have normalised blood sugar levels for relatively short periods in the preclinical diabetic rhesus model but have met with limited success in the stringent baboon model. Here we report that NICC from genetically modified (GM) pigs deleted for αGal and expressing the human complement regulators CD55 and CD59 can cure diabetes long-term in immunosuppressed baboons, with maximum graft survival exceeding 22 months. Five diabetic baboons were transplanted intraportally with 9,673 – 56,913 islet equivalents (IEQ) per kg recipient weight. Immunosuppression consisted of T cell depletion with an anti-CD2 mAb, tacrolimus for the first 4 months, and maintenance with belatacept and anti-CD154; no anti-inflammatory treatment or cytomegalovirus (CMV) prophylaxis/treatment was given. This protocol was well tolerated, with all recipients maintaining or gaining weight. Recipients became insulin-independent at a mean of 89 ± 39 days post-transplant and remained insulin-independent for 397 ± 174 days. Maximum graft survival was 675 days. Liver biopsies showed functional islets staining for all islet endocrine components, with no evidence of the inflammatory blood-mediated inflammatory reaction (IBMIR) and minimal leukocytic infiltration. The costimulation blockade-based immunosuppressive protocol prevented an anti-pig antibody response in all recipients. In conclusion, we demonstrate that genetic modification of the donor pig enables attenuation of early islet xenograft injury, and in conjunction with judicious immunosuppression provides excellent long-term function and graft survival in the diabetic baboon model.
334.8

**Extracellular Vesicles as Mediators of Infectious Tolerance in Human Alloreactive Regulatory Cells**

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**Introduction:** We have developed a method for ex vivo expansion of donor antigen specific T regulatory cell enriched lines (ASTRLs) from stable human kidney transplant recipients (KTRs). Rat derived ASTRLs induced prolonged graft survival and donor specific tolerance in a rat kidney transplant model. Human ASTRLs are suppressive in their phenotype and function. We examined the various mechanisms of ASTRL mediated suppression including extracellular vesicle (EV)-mediated suppression.

**Method:** ASTRLs were expanded ex vivo from PBMCs of stable KTRs by stimulation with donor allopeptides in presence of IL-2. ASTRLs were characterized for conventional Treg markers by flow cytometry. Functional characterization of ASTRLs were performed using standard suppression assays. Extracellular ATP hydrolysis was determined by malachite green assay. EVs were isolated from the ASTRL expansion media via differential ultracentrifugation and characterized by liquid chromatography-mass spectrometry.

**Results:** The suppressive mechanism of ASTRLs was alloantigen-specific and dependent on cell-cell contact as shown in Figure 1 (top panel). ASTRLs upregulated the expression CD39 and CD73, ectonucleotidases associated with the adenosinergic pathway, and ASTRLs demonstrated increased extracellular ATP hydrolysis (eATP) that was inhibited by POM1, a CD39 specific inhibitor (Figure 1 left bottom panel) which also abrogated the suppressive effect of ASTRLs. In KTRs ASTRLs specific for one donor alloantigen were able to suppress an effector response against other donor alloantigens demonstrating bystander/linked suppression and inhibit effector T cell proliferation in response to both direct and indirect allorecognition (Figure 1 bottom right panel).

EVs isolated from ASTRLs enhanced the suppressive ability of ASTRLs and hydrolyze eATP independently, which was inhibited by POM1 (Fig. 2) and increase production of IL-4, IL-13, and IL-1RA by alloantigen stimulated T cells, indicating a biasing towards a regulatory response (Fig. 2). Global proteomics identified 1,709 unique proteins in the large EV fraction and 1,356 unique proteins in the small EV fraction. Pathway analysis revealed that both EV fractions under stimulation were enriched for proteins involved in T cell receptor (TCR) signaling and Treg differentiation (Fig. 2) with 145 differentially enriched proteins (DEPs) in the large and 162 DEPs in the small EVs (q<0.05). Pathway analysis of DEPs will be presented.

**Conclusion:** ASTRLs expanded from stable KTRs suppress donor antigen specific effector responses predominantly via the adenosinergic pathway and demonstrate bystander/linkd immunosuppression. ASTRL-EVs enhance the suppressive capacity of ASTRLs and exhibit an increase in CD39 function. These findings indicate that human ASTRLs may be useful as autologous regulatory cell therapy in transplant recipients and that ASTRL related EVs may be useful adjuncts to ASTRL cell therapy.

Saxena Transplantation Fund.
Custom Bone Massive Allograft for Lower Limb Salvage Surgery, the Impact of Imaging and 3D Printing. Experience of the Tissue Bank of the Hospital Luis Vernaza (2016-2021)

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Introduction: Luis Vernaza Hospital tissue bank implemented the anatomical engineering service, which performs the activities of digitizing stored tissues, virtual surgical planning of custom tissues, and the generation of cutting guides for efficient osteotomies between donor and recipient. The main use of this technology is to provide allografts of the proximal tibia or distal femur for salvage surgery of the lower limb, with which it has been possible to restore the mobility and functionality of the knee to patients with bone tumors. With this technology, we have managed to deliver custom allografts with a discrepancy of 1 to 2 mm between the measurements of the recipient and that of the donor, in addition to obtaining three-dimensional measurements such as the curvature of the femoral condyle and the curvature of the femorotibial joint.

Objective: To present the results obtained by the anatomical engineering service in the development of custom fabrics for lower limb salvage surgery.

Materials and Methods: The complete knee joint, including 20 cm of the distal femur and 20 cm of the proximal tibia, is obtained from cadaveric donors. Then we proceed with the digitalization of the tissues using computed axial tomography, a service provided by the imaging center of the Luis Vernaza Hospital. At the time of requesting a graft, the specialist attaches the tomography of the recipient with the indications and measurements of the graft to be requested. The search for the graft is carried out with it in the digital catalog of the tissue bank and using the Mimics anatomical engineering software using segmentation in volumes, the approximate measurements between recipient donors are obtained. Analyzing the curvature of the femoral condyle and the surface of the tibial plateau. With the indicated stockings, we proceed with the processing of the tissue, extracting the required tissue and the ligamentous elements necessary for its subsequent fixation.

Results: Thanks to this technology, it has been possible to restore mobility to 10 patients aged between 15 and 56 years. The most frequent pathology was osteosarcoma (6) followed by giant cell tumor and metastasis from other sites. The most requested graft was the proximal tibia 6 requested units, distal femur 3 units, and 1 humerus. Approximately the amount of tissue replaced was 15 cm.

Discussions and Conclusions: It is difficult to obtain a synthetic replacement for the proximal tibia or distal femur, due to their multiple compositions (bone tissue, cartilage, and ligamentous fixing elements). Applying this technology to the tissue bank avoids the amputation of limbs due to lack of elements for reconstruction, because of which the allograft from a cadaveric donor with the exact stockings allows rapid restoration of the patient’s mobility and return to their usual activities.
Development and Evaluation of a Cell Therapy for Ex Vivo Porcine Kidney Graft Conditioning Using Exosomes Derived From Porcine Urine Progenitor Cells

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Introduction: Kidneys from extended criteria donors are particularly sensitive to ischemia/reperfusion injury. Among strategies to improve graft conditions, our study aims to test a cell therapy based on exosomes derived from porcine Urine Progenitor Cells (pUPCs) combined with Hypothermic Machine Perfusion (HMP) followed by Ex Vivo Normothermic Perfusion (EVNP).

Materials and Methods: pUPCs were isolated and characterized by flow cytometry, immunofluorescence and western blotting. pUPC-derived exosomes were extracted by ultracentrifugation and characterized by western blotting, electronic microscopy and Nanosight Tracking Analysis. Porcine kidneys obtained from slaughterhouse were submitted to 32 min of warm ischemia then preserved by HMP for 24 hours at 4°C. Afterwards, kidney early function recovery was assessed using EVNP for 5 hours at 37°C. For cell therapy, pUPC-derived exosomes were injected via the porcine kidney artery. Three experimental groups were planned (n=6/group): Group 1: HMP/vehicle + EVNP/vehicle; Group 2: HMP/ pUPC-derived exosomes + EVNP/vehicle; Group 3: HMP/ pUPC-derived exosomes + EVNP/ vehicle. Analyses include functional parameters, histology, biomarkers, protein/cytokine and gene expression analyses in tissue samples and HMP and EVNP perfusates, as well as perfusate effect on in vitro porcine aortic cell cultures.

Results: Firstly, pUPCs were successfully isolated and amplified from porcine urine samples. Isolated pUPCs expressed stem cell markers such as SSEA4 embryonic stem cell marker, CD90 mesenchymal stem cell marker and are negative for CD45 hematopoietic stem cell marker and CD31 endothelial marker. Cells expressed kidney channel water markers such as AQP1 and AQP2 and can gain epithelial phenotype when differentiated into tubular cells. pUPC-derived exosomes expressed Alix and TSG101 exosome markers and were of expected size (40-100nm of diameter) and delimited with a double membrane. Impact of exosome treatment during HMP and EVNP protocol is currently assessed. Preliminary results seem to show that pUPC-exosome injection seems feasible and does not induce acute kidney dysfunction. The potential beneficial effect will be assessed soon after the inclusion of the 18 porcine kidneys (15 performed for now).

Conclusion: This study is showing the feasibility to use porcine urine stem cells derived exosomes for renal graft conditioning, and will assess the impact of this therapy on kidney graft quality and early function.

Keywords: Kidney, Exosomes, Hypothermic machine perfusion, Ex vivo Normothermic perfusion, Stem cells, Cell therapy.

Belatacept and Sirolimus Immunosuppression Increases CD4+FOXP3+T-Reg and Central Memory Response in Islet-Transplantation

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Aims: To understand the innate and adaptive immunophenotype associated with maintenance immunosuppression with Tacrolimus and Mycophenolate or Sirolimus and Belatacept in islet-cell transplantation. To identify cell subsets associated with graft rejection and long-term insulin independence.

Methods: Of 18 islet-transplant recipients, 5 were treated with Belatacept and sirolimus maintenance immunosuppression. Whole blood flow-cytometric immunophenotyping was performed using 45 cell markers at pre-transplantation (0-months), then 0.5-, 1-, 3- and 12-months post-transplantation. Mean cell proportions between drug groups were compared at each time-point using Mann-Whitney U test, and against adult controls at 0-months. Non-parametric and regression analysis will be performed at 12-months comparing cell proportions against graft function according to the IgI’s criteria.

Results: Overall there was a significant decrease in CD2+T-cell count (p=0.007) at 12-months post-thymoglobulin induction. Eighteen cell proportions differed significantly between drug groups (Fig. 1). Absolute mean CD4:CD8 ratio was reduced in both groups and lower at all post-transplantation Belatacept timepoints. However, the CD4+FOXP3+T-regs (p=0.036) proportion was higher in the Belatacept group at 12-months, suggesting the agent spares this subset while deleting effectors. This effect was especially noticeable at 3-months where the absolute CD4+FOXP3+T-Reg count was higher in the Belatacept group. Central-memory CD62L+CD45RA- CD4+ T-cells were increased, while CD62L-CD45RA+ CD4+ T-cells decreased, suggesting an upregulated central-memory response. This was consistent with an increased proportion of CCR7+ compared to CCR7- CD45RA+CD4+ T-cells and an increased proportion of CCR7+central-memory CD25+FOXP3+T-regs.

Conclusion: Belatacept and Sirolimus use was associated with increased CD4+FOXP3+T-regs and an upregulation of the central memory response when compared to Tacrolimus and Mycophenolate.
Targeting CD47 Improves Insulin Secretion and Islet Transplant Outcomes

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Background: Type I diabetes mellitus is caused by autoimmune destruction of β-cells in pancreatic islets. Insulin replacement provides some management of glycemia but cannot provide normal metabolic control, which is only achievable with islet transplantation. Strategies that increase insulin secretion and islet cell survival can improve post-transplant outcomes. CD47 is a cell surface receptor that regulates cell stress responses, but its role in β-cell physiology is unknown. We investigated the impact of CD47 on islet function.

Methods: Human islets from the National Islet Transplant Consortium, primary murine islets, and MIN6 cells were investigated for CD47 expression, glucose-stimulated insulin secretion and ultrastructural changes. Islets and whole pancreas isolated from C57BL/6 (WT) and CD47KO mice (C57BL/6 background) were investigated for insulin secretory capacity. Syngeneic islet transplantation was performed using CD47KO or CD47-antibody-treated WT islets. Non-obese diabetic (NOD) mice were injected with CD47 blocking antibody.

Results: CD47 was expressed in islets and co-localised with insulin in the pancreas, MIN6 cells and primary murine islets. Hypoxia increased CD47 expression but reduced insulin production. Under electron microscopy, CD47KO islets demonstrated increased insulin granule docking and exocytosis compared to WT islets. Inhibition of CD47 expression via siRNA, morpholino oligonucleotide, or blockade with antibody, increased insulin secretion following glucose stimulation. This coincided with increased activity of known insulin regulatory proteins Lyn kinase (through increased phosphorylation) and Cdc42 (increased GTP-bound form). Compared to WT controls, CD47KO mice demonstrated improved glycemic control in response to a glucose load, and this finding was recapitulated following administration of CD47-antibody to WT mice. Transplantation of syngeneic CD47KO islets (Figure 1A) or CD47-antibody treated WT islets (Figure 1B) rapidly led to euglycemia in recipient animals, compared to WT islets alone. Treatment of NOD mice with CD47-blocking antibody delayed the onset of overt diabetes without altering insulitis scores.

Conclusion: CD47 levels can be manipulated to improve insulin secretion, and targeting CD47 pharmacologically represents a novel therapeutic strategy in type 1 and type 2 diabetes, as well as islet transplantation.
Development and Validation of an Artificial Intelligence Model for a Better Prediction of Hepatocellular Cancer Recurrence After Transplantation: A Retrospective International Study

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Background & Aims: Identifying patients at high risk for recurrence of hepatocellular carcinoma (HCC) after liver transplantation (LT) is a challenging issue. The present study aims to develop and validate an accurate post-LT recurrence prediction calculator using the machine learning method.

Methods: 3,326 HCC patients transplanted during the period 2000-2018 in 17 North American, European, and Asian centers composed the International Cohort. The external Validation Cohort consisted of 470 HCC patients transplanted at the Bologna University during the same period. The International Cohort was split to generate a Training and a Test Set (70/30%). Analyzing the Training Set data with a Cox proportional hazards deep neural network, the Time_Radiological-response_Alfetoprotein_Artificial-Intelligence (TRAIN-AI) model was developed. The Test Set and the Validation Cohort were used for internal and external validation of the model. The prognostic ability of the TRAIN-AI was compared to other currently available recurrence risk algorithms.

Results: The TRAIN-AI model showed very good c-statistics, with areas under the curve of 0.78 (95%CI=0.73-0.82) and 0.67 (95%CI=0.64-0.74) in the Test Set and the Validation Cohort, respectively. The TRAIN-AI always significantly outperformed the other scores in both the internal and external validation cohorts. Application of the TRAIN-AI model in individual patients allowed to calculate the expected recurrence after LT. Some examples of the application of the model are displayed in Figure 2, in which specific values of the seven variables composing the model were proposed.

The expected vs. the observed recurrence rates in the (A) Test Set and (B) Validation Cohort were investigated. In the Test Set, the calibration of the prediction model was excellent, with expected survivals that matched closely the observed survivals. In the Validation Cohort, the overall calibration of the prediction model was satisfactory.

Conclusions: The proposed TRAIN-AI score had a higher accuracy than other available criteria regarding post-LT recurrence risk. Further validation of the model is required. A web calculator has been developed to improve the user-friendly availability of the model (https://www.train-ai.ml).
Long-term Outcomes of Liver Transplantation Using Grafts From Donors With Active Hepatitis B virus Replication: A Multicenter Cohort Study

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Background: Liver grafts from donors with hepatitis B infection contributed to expanding the donor pool under the Hepatitis B Immunoglobulin (HBIG) and antiviral agents (NA: Nucleos(t)ide analogs) in the hepatitis B virus (HBV) endemic area. The purpose of this study is to describe the long-term outcome of liver transplantation (LT) using grafts from donors with active and chronic hepatitis B virus infection.

Methods: Between January 2000 and April 2019, 2260 liver transplants (LTs) were performed at Seoul National University (SNU) Hospital, SNU Bundang Hospital (SNUBH), and Seoul Metropolitan Government-SNU Boramae Hospital. Twenty-six (1.2\%) grafts from donors with HBsAg (+), HBeAb (+), or HBV DNA (+) were classified as active and chronic HBV hepatitis grafts and retrospectively reviewed. The demographics of donors and recipients, as well as the outcomes of transplantation, were analyzed. HBV reactivation has been defined as an increase in viral DNA in HBsAg (+) grafts and seroconversion of HBsAg positive grafts in chronic hepatitis grafts. Additionally, we used the chronic HBV infection stage to evaluate and manage recipients who received HBV-infected grafts.

Results: Sixteen LT were performed on deceased donors using active HBsAg (+) grafts. Ten living donor LT were performed using inactive HBV grafts; eight patients with inactive hepatitis; HBsAg (-), HBcAb (+), and HBV DNA (+), and two patients with chronic HBV hepatitis with seroconversion; HBsAg (-), HBsAb (+), and HBeAg (+) (Figure 1). The recipients were aged 59.0 ± 10.3 years and had a MELD score of 19.9 ± 8.4. The mean duration of follow-up was 82.6 ± 60.1 months. Depending on the donor and recipient’s serology, NA and HBIG were administered during the perioperative period. Deaths (n=8) occurred between 2.0 and 47.3 months following LT. All deaths were reported in DDLT. When compared with LT using grafts without HBV, LT using HBV infected grafts did not show any significant difference in patient survival (30.8\% vs. 18.6\%, p=0.247) (Figure 2). The most common causes of death were infection (n=4) and HCC recurrence (n=3). All recurred HCC patients died of cancer. HBV reactivation was identified in 1 patient but resolved spontaneously without additional management. All 10 LDLT recipients survived and were in good condition during follow-up. Survivors were in inactive or resolved status for HBV infection under the HBIG and NA. No graft failure was observed. Fourteen patients followed-up more than 5 years were stable and no increase in HCC recurrence rate was observed 5 years after transplantation.

Conclusion: Considering their long-term outcomes, liver grafts with active and chronic HBV infection can be safely used for LT in HBV endemic area.
Comparison of Outcomes of High Utilization Centers For Donation After Circulatory Death Liver Transplantation in the Acuity Circles Era

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Introduction: The recent acuity circles (AC) liver allocation policy in the United States has increased rates of donation after circulatory death (DCD) liver transplantation. We hypothesize transplant centers with high volume DCD graft usage may have differing outcomes.

Methods: All adult DCD transplant recipients in the UNOS STAR file from Jan 11 2016 to Sept 30 2021 were included. Living liver grafts, pediatrics, and non-kidney simultaneous transplantation were excluded. The top decile of DCD transplant centers by volume per year were identified. 6-month and 1-year patient and liver graft survival were compared to bottom 90% usage centers using propensity score matched fine gray regression models. Outcomes were stratified by pre-AC (1/11/2016-2/3/2020) and post-AC (2/4/2020-9/30/2020) eras. Transplant recipients that cross eras were censored on last day of the pre-AC era.

Results: 2299 DCD liver transplantation recipients were included in this study; 2012 in pre-AC and 287 in post-AC eras. High DCD volume (top decile) centers had significantly improved 6-month (HR: 0.32, 95% C.I.: 0.11-0.91, P = 0.033) and 1-year (HR: 0.42, 95% C.I.: 0.17-0.98, P = 0.043) patient survival in the post-AC era compared to bottom 90% centers by volume. No significant differences were noted in 6-month or 1-year liver graft survival in either era.

Conclusion: The top decile DCD transplantation volume center have improved 6-month and 1-year patient survival compared to lower volume centers with the introduction of the acuity circles policy in the United States.

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<td>Patient Death</td>
<td>Hazard Ratio: 0.605, 95% C.I. 0.31-1.10</td>
<td>Hazard Ratio: 0.42, 95% C.I. 0.19-0.91</td>
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<td>Liver Failure</td>
<td>Hazard Ratio: 0.79, 95% C.I. 0.53-1.21</td>
<td>Hazard Ratio: 0.41, 95% C.I. 0.25-0.69</td>
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<tr>
<td>Patient Death</td>
<td>Hazard Ratio: 0.76, 95% C.I. 0.42-1.35</td>
<td>Hazard Ratio: 0.44, 95% C.I. 0.18-0.97</td>
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<tr>
<td>Liver Failure</td>
<td>Hazard Ratio: 0.84, 95% C.I. 0.53-1.36</td>
<td>Hazard Ratio: 0.48, 95% C.I. 0.26-0.85</td>
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Propensity score matching estimating treatment effect of top 10% vs bottom 90% DCD utilization centers adjusting for: recipient age, sex, Karnofski score, blood type, BMI, life support requirement at transplant, ventilatory requirement at transplant, cause of liver disease, recipient encephalopathy at transplant, recipient history of cancer, recipient race, recipient history of previous transplant, history of PVT, history of abdominal surgeries, MELD score at transplant, donor age, donor sex, donor blood type, donor BMI, cold ischemia time, warm ischemia time, PPD/HiR risk donor, donor cause of death, donor dialysis requirement at transplant. Patient matched to each group by propensity score to its neighbor by nearest Mahalanobis distance in a 1:1 manner within a caliper of 0.20 standard deviations.
Use of Donation After Circulatory Death Donors for High Model for End-Stage Liver Disease Recipients

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Background: Donation after circulatory death (DCD) for liver transplantation (LT) remains an underutilized option in the United States, especially for the sickest end-stage liver disease patients. We hypothesized that recipients with a Model for End-Stage Liver Disease (MELD) ≥35 may have acceptable outcomes after DCD-LT.

Methods: We collected and analyzed data on adult DCD recipients from the University of California, San Francisco (UCSF) cohort who had a lab-MELD of ≥35 at listing (n=41). No machine perfusion was used. We compared survival (Kaplan-Meier and Log Rank test) with our historical donation after brain death (DBD) recipients who had a lab-MELD of ≥35 at transplant (n=1,918).

Results: DCD recipient age (±SD) was 55.4 (8.8) years old, 63.4% were male, leading reasons for transplant were hepatitis C (34%) and alcoholic cirrhosis (27%). BMI (±SD) was 28.9 (6.6). All recipients were hospitalized prior to transplant, 46% were in the intensive care unit, and 51% were on renal replacement therapy at the time of transplant. 17% underwent a simultaneous liver-kidney transplant. Donor age was 55.4 (8.8) years old, 63.4% were male, and the average BMI was 25.6 (6.8) kg/m2. Donor warm ischemia time was 21.0 (5.2) min, liver extraction time was 45.3 (19.3) min, and cold ischemia time was 7.8 (2.3) hours. The median length of stay post-transplant was 10 days. One patient out of four (26.8%) was on dialysis at discharge.

Conclusion: DCD transplant in MELD of ≥35 recipients is feasible and can achieve similar one-year survival rates compared to DBD recipients with MELD≥35. Ischemic cholangiopathy remains present at an expected rate.

Conclusions: Although GS after re-LT has improved over time, the HR of Re-LT stayed high and did not show clear improvement.

Has the Risk of Liver Re-Transplantation Improved Over the Two Decades? A UNOS Data Analysis

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Introduction: Liver transplantation (LT) is an established treatment option for end-stage liver disease and post-LT outcomes have improved over the two decades. Despite of accumulation of knowledge and improvement of surgical techniques, liver re-transplantation (re-LT) remains a challenging operation, and reported 1-year survival of re-LT is nearly 15% less compared to initial LT in US registry data. Controversy exists regarding indications for re-LT in the context of organ scarcity and the significantly higher chance of organ loss in re-LT. However, re-LT is the only life-saving option for patients with failing liver grafts. The aim of this study was to elucidate whether re-LT outcomes have advanced with experience over the last two decades.

Methods: This study used 134,254 adult patients in the United Network for Organ Sharing (UNOS) database from 2003 to 2020, evaluating the characteristics and outcomes of 6,689 (5.0%) re-LT patients. Re-LT patients were grouped by 3-year intervals to investigate the chronological evolution of re-LT. Postoperative outcomes were evaluated by graft survival (GS) at 30 days, 90 days, and 1-year after transplantation. Cox proportional hazards models were used to assess the hazard ratio (HR) of re-LT. The chronological changes of HRs of re-LT were plotted and compared to donation after cardiac death (DCD) LT.

Results: The case numbers of re-LT did not increase over time, despite increases in overall LT volume (Figure 1A). Both waiting time and median MELD at the time of re-LT gradually increased, while the percentage of re-LT for hepatitis C decreased significantly over time (Figure 1B-D). The changes in 30-day, 90-day, and 1-year GS between initial and re-LT decreased over time (2003-2005: 91.7%, 88.1%, and 79.9% vs. 84.2%, 77.1%, and 66.9%, respectively; 2018-2020: 95.9%, 94.1%, and 89.9% vs. 91.0%, 86.7%, and 81.3%, respectively; Figure 2A). The effect of transplant era was examined by comparing HRs between re-LT and DCD LT (Figure 2B). Although graft outcomes of LT using DCD have improved over time, the HR of Re-LT stayed high and did not show clear improvement.

Conclusions: Although GS after re-LT has improved over time, interestingly, the HR of re-LT has not improved with experience. Meanwhile, the HR of using DCD donors in LT has clearly improved over time. These results suggest that the overall re-LT outcomes maybe have improved through strategy optimization in donor-recipient selection, but the adverse prognostic influence of re-LT has not improved despite advancements in LT over the last two decades.
Long-term Outcomes of Living Donor Versus Deceased Donor Liver Transplantation for Acute Liver Failure in United States

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Introduction: Acute Liver Failure (ALF) is rarely encountered but often is associated with high morbidity and mortality. Timely Liver Transplantation is universally the only accepted rescue therapy, but not much is known about the usage of Living Donor (LDLT) versus Deceased Donor (DDLT)Liver Transplantation in the United States for this indication.

Method: United Network of Organ Sharing (UNOS)/ Organ Procurement and Transplantation Network (UNOS/OPTN) data was reviewed from January 2002 to December 2020. Adult and pediatric recipients with diagnostic codes for ALF and listed as Status 1 were included in the study. Clinical, laboratory, and demographic characteristics were compared between LDLT and DDLT groups.

Results: There were a total of 246 LDLT (3.8%) and 6153 DDLT (96.2%) recipients with the diagnosis of ALF (Table 1). There was a difference in age and gender between the groups, with 93.5% of LDLT cases being for pediatric ALF cases versus 45.9% of DDLT cases being for pediatric recipients of age less than 18. There were more female gender in the DDLT group. Race was not different between the two groups. The proportion of patients waiting ≥ 3 days was 64.1% in LDLT compared to 77.2% in the DDLT group (P<0.001). There was no statistical difference between the two groups in terms of sodium, bilirubin, and INR. There were more patients with hepatic encephalopathy, and on renal replacement therapy in the DDLT group compared to LDLT group. Overall, 1, 5 and 10 year overall survival among the recipients with the diagnosis of ALF was similar between LDLT and DDLT groups, 87.7% vs. 85.5%, 81.1% vs. 81.1%, 74.7% vs. 73.3% (P=0.16) (Figure 1) (Log rank P=0.16).

Conclusions: In the US, LDLT constitutes of only 3.8% of all liver transplants for ALF. In addition, LDLT was mostly used among pediatric recipients (93.5%), whereas DDLT was mostly used for adult recipients (54.1%). Signs of decompensation with hepatic encephalopathy, ascites, and on renal replacement therapy were more common in DDLT than LDLT group. LDLT can be carefully considered in a select group of adult ALF cases, in early phases, before further progression into renal failure and advanced encephalopathy.

Spatial Transcriptomic Profiling Reveals Immunosuppression And Immunosenescence-Driven Skewing of Immune Response in Cutaneous Squamous Cell Carcinoma Immune Response in Kidney Transplant Recipients, Associating With Adverse Cancer-Related Outcomes

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Introduction: Cutaneous squamous cell carcinoma (SCC) is the most common malignancy in immunosuppressed populations, demonstrating increased aggression compared to the general population. One such immunosuppressed group is organ transplant recipients. We previously demonstrated peripheral blood markers of immune ageing (immunosenescence) identifies kidney transplant recipients (KTR) with poorer cancer-related outcomes, with earlier SCC recurrence and greater risk of metastatic SCC/non-keratinocyte malignancy development which remains significant after multivariate correction. We sought to explore the mechanism underlying this association.

Methods: Excised SCCs from KTR (n=16) and non-immunosuppressed controls (NIC, n=11) were assessed by immunohistochemistry to quantify infiltrating T cell populations. High-resolution spatial transcriptomic profiling was utilised to evaluate alterations in gene expression and transcriptomic pathways (using gene set enrichment analysis using the Reactome knowledgebase) within the tumour and immune-rich peritumoural regions of SCC excised from KTR using the 1800-gene ‘Cancer Transcriptome Atlas’ on the Nanostring GeoMx platform (n=6).

Results: CD8+ and FOXP3+ tumoural T cell density decreased with advancing peripheral blood immunosenescence in KTR but not in NIC on immunohistochemistry. Across the KTR cohort, upregulation of pathways in the peritumoural infiltrate relating to TCR signalling, co-stimulation, chemotaxis and immunoregulation was seen compared to the tumour bed (Figure 1A). Within immunosenescent KTR, there was greater enrichment of pathways relating to chemotactic signalling and phagocytosis were seen (Figure 1B). Cellular deconvolution revealed enhanced accumulation of macrophages with an M2 gene signature, associating with reduced monocyctic dendritic cell and CD8+ T cell density (Figure 1C).

Conclusion: We conclude that immunosenescence synergises with iatrogenic immunosuppression in cutaneous malignancy, leading to skewing of the immune milieu culminating in accumulation of suppressive M2 macrophages and associating with adverse cancer-related outcomes. Quantification of immunosenescence in KTR may permit risk stratification facilitating potential preventative interventions.

The work presented here was supported by grants from the Wellcome Trust, British Skin Foundation, Oxford Hospital Charities and Chinese Academy of Medical Sciences (CAMS) Innovation Fund for Medical Science (CIFMS), China (grant number: 2018-I2M-2-002).
Elevated Donor-Derived Cell-Free DNA (Dd-cfDNA) in the Early Post-transplant Period Is Associated With an Increased Incidence of Adverse Clinical Outcomes in Kidney Transplant Recipients

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Introduction: Early post-transplant elevations in dd-cfDNA, even in the absence of histologic rejection or other overt pathology, have been suggested to carry a risk of adverse outcomes among solid organ transplant recipients. We investigated this association among kidney transplant recipients enrolled in the Kidney Allograft Outcomes AlloSure Registry (KOAR, NCT03326076).

Methods: To assess the impact of early post-transplant dd-cfDNA elevations, we evaluated the incidence of a clinical composite that included biopsy-proven rejection (BPAR), detection of de novo donor specific antibodies (dnDSA) and return to dialysis in patients with and without median dd-cfDNA ≥1% over the first 100 days post-transplant. Patients with events before day 100 were excluded. Univariate and multivariate analyses were performed.

Results: 51 of 1296 patients (3.9%) had a median dd-cfDNA ≥1.0% during the first 100 days post-transplant. In a univariate model, these patients had a significantly higher risk of the experiencing both the composite outcome and each individual component during the first post-transplant year (Figure 1). In a multivariate Cox proportional hazards model that included recipient age, delayed graft function, donor type (living vs deceased), and recipient sensitization, only 100-day median dd-cfDNA elevation ≥1.0% was a statistically significant predictor of the composite outcome, with a hazard ratio of 2.99 (95% CI: 1.59 - 5.61, p < 0.005) (Table 1).

Conclusions: Our findings suggest that early post-transplant elevations in dd-cfDNA among kidney transplant recipients, even in the absence of clear-immunologic or histologic correlates, identify a population of patients at risk for adverse clinical outcomes during the first post-transplant year. Molecular risk-stratification using dd-cfDNA may have implications for clinical surveillance and therapeutic management of these patients.

Table 1: Risk Factors for Composite of Rejection, dnDSA, and Return to Dialysis in the First Post-Transplant Year

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median 100-day dd-cfDNA ≥1.0%</td>
<td>2.99</td>
<td>1.59 – 5.61</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>Age (continuous)</td>
<td>1.00</td>
<td>0.98 – 1.01</td>
<td>0.62</td>
</tr>
<tr>
<td>Delayed Graft Function</td>
<td>1.55</td>
<td>0.38 – 6.37</td>
<td>0.54</td>
</tr>
<tr>
<td>Deceased Donor</td>
<td>1.22</td>
<td>0.77 – 1.95</td>
<td>0.40</td>
</tr>
<tr>
<td>Recipient Sensitization (p&lt;0.5)</td>
<td>0.87</td>
<td>0.59 – 1.28</td>
<td>0.47</td>
</tr>
</tbody>
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Clinical Utility of Donor-Derived Cell-Free DNA During the Period of Recovery of Renal Function After Kidney Transplantation

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Purpose: This study evaluates the clinical utility of monitoring donor-derived cell-free DNA (dd-cfDNA), a biomarker of kidney injury, in recipients of high Kidney Donor Profile Index (KDPI) transplants during the period of kidney function recovery.

Methods: This is a single center, prospective, cohort study in recipients of high KDPI kidneys who developed delayed graft function (DGF), defined as the need for dialysis within the first week after transplantation. All patients received a single 3 mg/kg anti-thymocyte globulin dose, tacrolimus, mycophenolate, and prednisone. Blood samples were obtained at 14 (D14) and 30 (D30) days to measure the percentage (%) of dd-cfDNA. The dd-cfDNA > 1% is associated with increased probability for acute rejection (AR).

Results: This preliminary analysis includes data from 69 patients. The median KDPI was 73% (IQR 47-87) and the mean cold ischemia time was 27±7 hours. The incidence of DGF was 89.8% with a median duration of 6 (IQR 2-9) days. At D14 the median GFR was 12 ml/min/1.73 m2 (IQR 0.02-0.78), with 19 patients (29%) showing dd-cfDNA >1%. Surveillance biopsies during DGF were performed in 42 (61%) patients showing one T-cell mediated rejection IA (dd-cfDNA of 0.41%) and 4 borderline changes (dd-cfDNA 0.82%, 0.85%, 0.98%, 1.90%). Using dd-cfDNA >1% to guide the indication of the surveillance biopsy, we would have avoided 22 (52%) biopsies but missed 2 (2%) patient with AR. At D30, the median GFR was 36 ml/min/1.73 m2 (IQR 28-48) and the median dd-cfDNA levels were 0.40% (IQR 0.01-0.66), with 12 patients (19%) showing dd-cfDNA >1%. Surveillance biopsies performed in 21 (30.43%) patients with incomplete recovery of kidney function showed 4 borderline changes (dd-cfDNA 0.17%, 0.66%, 0.67%, and 2.80%). Using dd-cfDNA >1% to guide the indication of the surveillance biopsy, we would have avoided 12 (57%) biopsies without missing any AR episodes. Overall, 5 (7%) patients showed dd-cfDNA >1% at D14 and D30, but none of them showed biopsy confirmed AR.

Conclusions: This preliminary analysis suggests that monitoring dd-cfDNA may assist clinical decision during the period of DGF and in kidney transplant recipients with incomplete recovery of graft function.

Development and Validation of an Integrative dd-cfDNA System to Predict Allograft Rejection: A Population Based Study

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Introduction: Post-transplantation patient care requires development and validation of non-invasive biomarkers to improve allograft monitoring and prevention from unnecessary biopsies. Preliminary reports have suggested the association of donor derived cell-free DNA (dd-cfDNA) with allograft rejection. However, there is no proof of its added value beyond standard of care patient management in large and deep phenotyped cohorts.

Method: 1210 concomitant evaluations of allograft histology, anti-HLA DSA and functional parameters between 2013 and 2018 were included corresponding to 637 evaluations in the derivation cohort and 573 in the validation cohort. dd-cfDNA was measured in plasma at the time of the evaluation. Diagnoses were assessed using Banff 2019 criteria. Parameters associated with kidney allograft rejection were assessed using univariable logistic regression. We developed a risk model using the variables that were independently associated with rejection.

Results: Higher levels of dd-cfDNA were observed for AMR and TCMR or both compared to other diagnoses (Figure.1A). We found increments of dd-cfDNA levels with increasing Banff lesion scores for g, ptc, i, t, cg and C4d (Figure.1B). There was no association of dd-cfDNA levels with allograft inactive lesions. In multivariable analysis, dd-cfDNA (p<0.0001) was associated with kidney allograft rejection independently of DSA (p<0.0001), eGFR (p=0.018), kidney allograft instability (p=0.013) and previous rejection (p<0.0001). Based on these parameters, we built an integrative dd-cfDNA model that showed good discrimination (AUC: 0.83), good calibration, and added value beyond a model without dd-cfDNA (AUC of the model without dd-cfDNA: 0.77 vs 0.83 for the integrative model; p<0.0001). We confirmed our results in the validation cohort with a good discrimination (AUC: 0.82) and a good calibration. This integrative score including the dd-cfDNA is being validated in Belgium and in the US.

Conclusion: We demonstrate the independent and added value of dd-cfDNA in addition to conventional features to predict rejection. This first integrative system shows improved performance for patient monitoring and could help physicians in decision-making process.
Novel Drug Target Identified for Reversal of Renal Tubular Injury

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Purpose: Understanding the unique susceptibility of the human kidney tubule to oxidative cell stress and to identify compounds to support reversal of renal tubular damage.

Methods: To study the mechanisms of cell stress in renal tubular injury and identify novel drug targets for reversal, we utilized a study model of evaluating transcriptional profiles and cellular injury mechanisms in renal proximal tubule cells (RPTECs) isolated from the urine of patients with genetic confirmation of nephropathic cystinosis. Lysosomal fractionation, immunoblotting, confocal microscopy, intracellular pH, transmission electron microscopy (TEM), seahorse, and mitochondrial membrane integrity assays were performed; for additional validation, a CRISPR, cystinosin (CTNS)-/- RPTECs was generated. A new compound ATX was identified based on functional analysis against an FDA approved drug database and further evaluated for the rescue of the CTNS-/- RPTEC phenotype.

Results: Alterations in cell stress, mitochondrial reactive oxygen species (ROS), pH, autophagic turnover, and lysosomal and mitochondrial energetics, highlighted key changes in ATP synthases and vacuolar(V)-ATPases in patient-derived and CTNS-/- RPTECs. ATP6V0A1 was significantly downregulated in RPTECs from patients with nephropathic cystinosis and CTNS-/- RPTECs. ATP6V0A1 overexpression and/or ATX treatment rescued cell stress and mitochondrial function in CTNS-/- RPTECs.

Conclusions: Loss of cystinosin in CTNS-/- RPTECs results in decreased ATP6V0A1 expression, which changes intracellular pH, mitochondrial integrity and function. ATX can rescue these injured RPTECs through upregulating ATP6V0A1 expression and offers a potential novel therapeutic for limiting renal tubular injury. Application of ATX for murine models of renal transplant rejection, are underway to evaluate the efficacy of ATX in reversal of tubular injury and restoration of renal function.
Pretransplant Kidney Transcriptome Captures Immune Pathways and Predicts 24-Month Outcomes

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Introduction: The field of transplantation is in critical need of more accurate tools to predict allograft outcomes. A transcriptomic profile serves as a snapshot of the temporary cell state and thus, analyzing pretransplant kidney biopsies can provide detailed information on the early biological processes associated with posttransplant outcomes. Currently, there are no established predictive biomarkers for posttransplant kidney function.

Methods: Gene expression measurements were performed using Affymetrix GeneChip microarrays (HG-U133A 2.0) in the training set (n=174). Patients with low function had an eGFR <45 mL/min/1.73m2 (avg slope = -6.36 ml/min/1.73m2/year) and those with high function had an eGFR ≥45 mL/min/1.73m2 (avg slope= 0.81 ml/min/1.73m2/year) at 24 months. To identify differentially expressed genes (DEGs) and clinical characteristics associated with 24-month graft function, linear models were fit adjusting for surrogate variables. The performance of DEGs and clinical characteristics was assessed using the area under receiver operating characteristic curves (AUROC). A subset of candidate genes was measured in an independent set of pretransplant biopsies (n=96) using qPCR. A risk score equation was derived from the predictive model and performance was compared to KDPI.

Results: Donor age, race, and BMI correlated with 24-month function (p<0.05). No recipient characteristics were statistically significant between groups. Nearly 700 DEGs were found to be associated with 24-month outcomes (FDR<0.05). Grafts with low 24-month function showed upregulated genes related to immune responses (e.g., CD3D, CD69, CCL5, CXCR4, C1QB, FCER1G, ILR7) and downregulated genes related to metabolic/tubular functions (e.g., ENO1, FH, POGK, SLCO2A8, SLAA4, WDR1) (Fig 1A). Cell-type enrichment analyses identified monocytes, dendritic, myeloid, and natural killer cells as the main cell sources for the upregulated genes (Fig 1B). Using a 55 gene model adjusted for donor age, race, and BMI resulted in an AUROC=0.996 (KDPI AUROC=0.705). In the validation set, 13 genes + 3 donor characteristics (G+D) achieved an AUROC=0.821 (KDPI AUROC=0.691) (Fig 1C). Using a probability equation derived from the G+D model to predict low 24-month function, the sensitivity was 88.9% and the specificity was 66.6%. When using KDPI, the sensitivity was 80.6% and the specificity was 53.3% (Fig 1D).

Conclusion: This study represents the largest high-throughput transcriptomic analysis of pretransplant donor kidneys predicting 24-month outcomes. A predictive risk score was developed, which combines donor age, race, BMI, and donor quality gene markers, and can be calculated prior to transplantation to predict graft function. Differential pretransplant transcriptional profiles between kidneys with low and high function at 24-months were also identified, providing a deeper insight into the early biological processes leading to graft dysfunction.

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17beta-Estradiol and Methylprednisolone Associated Treatment Modulates Early and Late Cytokine Release in Lungs From Female Rats Submitted to Brain Death

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Introduction: Brain death (BD) causes hemodinamic and immunological alterations that compromise organs quality and viability. Compared to other organs, lungs have the lowest usage rate due to increased vulnerability during retrieval. After BD, lungs from female donors transplanted to male recipients present worse prognostics in comparison to organs from males donors. This is correlated with a higher inflammatory response in females, associated with the acute reduction of female sex hormones. Also, glucocorticoids are hormones known to influence the inflammatory response and, in females, evidence suggests that the presence of both estradiol and glucocorticoids is important to secure an appropriate response to inflammation. The aim of this study is to evaluate the associated treatment of E2 and methylprednisolone (MP) in female rats after BD.

Methods: Female Wistar rats were used and BD was induced by fast inflation of an intracranial balloon catheter. The animals were maintained for 6h. Rats received MP (MP, 4 mg/ml i.v–2 ml/h) or MP and E2 (MP/E2, 50 ug/ml i.v–2 ml/h) after 3h of BD until the end of experiment. As controls, we used non-BD animals (sham-operated (S)). Lung samples were collected after 6h for tissue homogenate, explant (lung tissues kept in culture medium for 24h), and relative gene expression analyzes. IL-1α, IL-6, TNF-α and CINC-1 were quantified in homogenate and explant samples. In parallel, IL-1β, IL-6 and TNF-α gene expression was also evaluated.

Results: In lung tissue homogenate, BD increased IL-6 after 6h and the two hormones associated treatment was able to reduce this cytokine (p<0.028). Both treatments were capable of reducing IL-1β (p<0.005). There were no differences among groups in CINC-1 and TNF-α concentrations. In lung culture, MP/E2 treatment reduced IL-1β (p=0.029) and CINC1 (p=0.007) and both treatments reduced IL-6 (p=0.002). As also observed in homogenate samples, there was no difference in explant TNF-α levels. Moreover, lung relative gene expression of IL-1β was reduced by both treatments (p=0.020). Despite being increased after BD, TNF-α gene was not altered by the treatments and no differences were observed in IL-6 gene expression.

Conclusion: These data suggests that the associated administration of E2 and MP after BD has anti-inflammatory effects by reducing the release and expression of cytokines and chemokines, especially IL-1β, IL-6 and CINC1, right after BD and 24h hours later, as seen in the explant analyzes. These results suggest that, in females, the association of corticoids and estrogens is a potential therapy option to improve organ quality.

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Comparison of Hypothermic Static and Normothermic Ex-situ Donor Heart Preservation in Heterotopic Heart Transplantation With the Murine Model

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Introduction and Background: Hypothermic static and Normothermic ex-situ preservation methods are the most widely used preservation technique worldwide. While cold static storage is associated with subsequent ischemic injury, Normothermic perfusion preservation has the potential to elogate preservation time with less ischemia. The current study compares the hypothermic and normothermic preservation methods in terms of graft performance, morphologic changes, and acute immune response in an experimental model.

Materials and Method: Twenty-five rats underwent heterotopic abdominal heart transplantation after two hours of donor heart hypothermic storage (HT group; n=10) or normothermic ex-situ preservation (NT group; n=15). Blood samples were obtained just before and after 4-hours of implantation to analyze surface markers of immune cells (CD4, CD8, CD161, CD45R). ECG and Echocardiography were performed before harvesting and after implantation. Hearts were extracted after four hours of implantation for Hematoxylin-Eosin (HE) and TUNEL-staining, and recipient rats were euthanized.

Results: 19 (76%) rats successfully survived after implantation (HT group: 100%, NT group: 60%). The mean ischemic time of the donor heart was 162.7±3.34 minutes in the HT group and 45±3.7 minutes in the NT group. The NT group showed no significant change in the heart rate before and after implantation but significantly decreased in the first hour of implantation in the HT group (259.5±24.3rpm) and normalized at 3 hours (338.3±34.1rpm). Ejection fraction and fractional shortening significantly decreased after implantation in both groups but were less significant in the NT group (P<0.001). Granulocyte was less significantly increased in the NT group compared to the HT group after the experiment (p=0.037). Although the gross structure was well preserved in both groups in HE-staining, the number of TUNEL positive cells was significantly higher in the HT group.

Conclusions: Our findings suggest that normothermic ex-situ preservation is associated with well-preserved donor hearts but similar recipient immune response in comparison with hypothermic static preservation.
Effects of Tacrolimus on Mechanical and Humoral Determinants of Brain Death-Induced Lung Injury

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Background: Donor brain death-induced lung injury may compromise graft function after transplantation. The mechanisms of this particular form of neurogenic lung edema and its possible prevention by immunomodulator Tacrolimus remain incompletely understood.

Methods and Results: Brain death was induced, by slow intracranial infusion of blood, in anesthetized pigs after randomisation to placebo (n=9) or to Tacrolimus (n=8). One, three, five and seven hours after brain death, pulmonary artery pressure (Pap), wedged Pap (Papo), right atrial pressure (Pra), effective pulmonary capillary pressure (Pcap), systemic artery pressure (Psa) and thermodilution cardiac output (Q) were measured. Blood and lung tissue were sampled and lung injury scored on pathological examination.

Brain death was associated with marked increases in Pap, PVR and Pcap, decreases in Psa and Q with growing need for Noradrenaline while Ppao and Pra remained in a physiological range. Arterial O2 pressure to fraction of inspired O2 (PaO2/FiO2) decreased. Brain death was associated with increased lung injury score together with increased gene expressions of interleukin (IL)-6 and IL-1β, heme-oxygenase-1, signal transducer and activator of transcription-3. Lung tissue pro-inflammatory IL-6/IL-10 ratio was decreased and pro-apoptotic Bax/Bcl2 ratio was increased. Tacrolimus partially corrected pulmonary hypertension and lung tissue biological perturbations. PaO2/FiO2 was inversely correlated to PCP and lung injury score. Serum IL-6 and IL-1β were correlated to PCP.

Conclusion: Brain death induced lung injury is related to effective pulmonary capillary hypertension with normal PAWP and pro-inflammatory and pro-apoptotic biological changes all partially reversed by preventive Tacrolimus treatment.

Figure: Hematoxylin-Eosin and TUNEL staining of HT and NT groups. A, B, E, F represent HE-staining, and C, D, G, H represent TUNEL-staining. Black arrows indicate TUNEL positive cells. (TUNEL, terminal deoxynucleotidyl transferase-mediated dUTP nick end labelling)
Tacrolimus for Prevention of Right and Left Ventriculo-Arterial Coupling Changes in Experimental Brain Death
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Purpose: Right ventricular (RV) dysfunction remains the leading cause of early mortality after cardiac transplantation. Tacrolimus (FK506) is an immune suppressor that could preserve heart function via its anti-inflammation effect in animal models. We sought to determine whether Tacrolimus might prevent brain death-induced RV dysfunction, and biological changes in myocarditis caused by BD acting on inflammation and apoptosis.

Methods and Results: After randomisation to placebo (n=9) or to Tacrolimus (n=8; 0.05 mg.kg⁻¹.day⁻¹), seventeen pigs were assigned to a brain death procedure. One, three, five and seven hours after Cushing reflex, the animals underwent hemodynamic evaluation. After euthanasia of the animals, myocardial tissue was sampled. This was repeated in a control group (n=7). Seven hours after Cushing reflex, brain death had resulted in increased pulmonary artery pressure (29.2±2 versus 19±1 mmHg) and in a 33%-decreased RV ratio of end-systolic to pulmonary arterial elastances (Ees/Ea), while left ventricle (LV)-arterial coupling did not change. This was prevented by Tacrolimus. Brain death-induced RV dysfunction was associated with increased RV expression of interleukin(IL)-6/IL-10, IL-1β, receptors for IL-1 and IL-6, b-3 adrenergic receptor, Toll-like receptor (TLR)-4 and neutrophil infiltration, while b-1 adrenergic receptor, TLR-2 and NLR family pyrin-domain-containing-3 expressions decreased. RV but not LV apoptosis was confirmed by TUNEL staining. Tacrolimus pre-treatment prevented RV-arterial uncoupling and changes in RV expression of IL-1 R, IL-6 R, RV apoptosis, as well as in neutrophil infiltration.

Conclusions: Brain death-induced isolated RV dysfunction is associated with RV activation of inflammation and apoptosis, partly by Tacrolimus.

Lung Donors After Circulatory Death: An Alternative of Low Technical Difficulty That May Potentially Increase Transplanteligible Lung Availability
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Introduction: Donor shortage is the main hindrance for achieving full development of Lung Transplant Programs. Donation after circulatory death (DCD), not yet widely used in Latin America, is a potential supply alternative to increase the availability of organs. The DCD Lung Donation Program designed for Uruguay is presented here.

Method: To establish such type of a program, it is deemed necessary to have: a National Transplant Organization, appropriate legislation, an approved ethical framework and specialized teams of professionals. In Uruguay, organ donation and transplantation is governed by the National Institute of Donation and Transplantation (INDT). Under Law 14005, organs are allowed to be used for therapeutic purposes once irreversible pathological changes deemed incompatible with life are confirmed. The Ethics Committee has agreed that the treating physicians (independent from INDT) are those responsible for confirming the patient’s decease upon a cardiac arrest, and once CPR procedures have proved unsuccessful. Upon confirmation of patient’s decease, DCD lung donation is considered. INDT is called in, being responsible for donor selection (Table 1) and conducting the legal procedures. 500 units/kg of heparin are administered plus 10 cycles of closed cardiac massages. 300 cc of venous blood are then extracted, which are stored in a transfusion blood bag. Samples are taken for serology purposes, routine procedures and chest x-ray performed. Chest tube placement in each hemithorax, second intercostal space, clavicular middle line. Maximum time between the cardiorespiratory arrest start and tube placement: 120 minutes. 6 litres of Perfadex® preservation solution or cool normal saline at 4 ºC is then introduced in each hemithorax. Next, Ventilator is switched-off. This way, the collapsed lung is maintained cool in a preservation solution until lung is removed in the operating room. Maximum time between topical preservation starts and lung removal begins: 240 minutes. Inside the operating room, drainage of both hemithorax is conducted. Ventilation starts at FiO2 100% and 5-cm H2O PEEP. Bronchoscopy is performed if needed. Cannulation of pulmonary artery and drainage of left auricle. Lavage is performed until clear liquid is obtained. Infusion through pulmonary artery of venous blood previously extracted with E2 prostaglandin. Blood gas is then extracted at the entrance, through the pulmonary artery and the affluent of each of the lung veins. If PaO2 difference between both samples is > 300 mmHg, then these are transplant-eligible organs. Organ procurement and preservation is done through normal procedure.

Results: Protocol is approved by INDT and Ethics Committee. Its implementation has been delayed due to COVID pandemic.

Conclusion: These DCD programs do not imply technical complexities, but they do involve organization and procurement challenges. They are an alternative to increase the number of organs suitable for transplantation.
Ultrasound Scanning in Lung Procurement. Protocol For Decision-Making With the Purpose of Increasing Transplant Eligible Lungs

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Introduction: Despite having a similar population, Latin America performs 11x less lung transplant procedure than Europe. Improving brain death diagnosis and converting potential donors into real donors is key to improve these numbers. Ultrasonography (US) is common practice in Intensive Care Units. Available literature on its use in the management of brain death donors and lung procurement is extremely scarce. The selection and rejection of lungs for transplantation is usually done with chest X-rays, however US has shown better sensitivity and specificity for the diagnosis of pulmonary pathologies. Lung US allows to identify the reversible causes low PaO2/FiO2 ratio (PaFi), thus allowing to establish specific interventions which, if proved successful, could turn lungs into transplant-eligible lungs.

Methods: Introducing a simple Protocol aiming at identifying and treating the main reversible causes of a low PaFi. Respiratory causes of a low PaFi ratio can be either parenchymal or pleural. Parenchymal causes: Pulmonary edema (either neurogenic or cardiogenic) determines the visualization of bilateral and symmetrical B lines. Fluid restriction prioritizing isotropic drugs to revert hypotension and usage of hypertonic solutions can reduce edema. Atelectasis, contusion and pneumonia can appear as patterns for unilateral B lines and/or consolidations. The presence of a static or dynamic air bronchogram can differentiate them. In atelectasis, fiberoptic bronchoscopy can be easily diagnosed through an ultrasound scan, not there being a reason for rejection. Its resolution can turn these lungs into transplant eligible lungs. The pneumothorax —frequently anterior in ventilated patients in dorsal decubitus— may be overlooked in the chest x-ray. Diagnosis is made by the absence of pleural sliding and presence of a lung point. Pleural effusion is anechoic, present quad sign and the sinusoid sign. The acquisition of skills to diagnose all these conditions does not require much reading and has a fast-learning curve (25 cases monitored).

Results: This Protocol is currently used for donor decision-making and will be implemented prospectively by the lung transplant team to assess its ability to increase the number of lungs suitable for transplantation.

Conclusions: US is a useful technique to identify reversible and treatable causes of a low PaFi, helping decision-making to increase the number of transplant eligible lungs.

Pneumatosis Intestinalis After Lung Transplantation: A Singlecenter Case Series

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Introduction: Pneumatosis intestinalis (PI) is a rare complication of transplantation, occurring in up to 5% of lung transplant recipients. PI is a radiographic finding of uncertain significance, and though generally considered benign in transplant recipients, often leads to unnecessary surgical interventions. While a correlation between high doses of immunosuppressants and PI has been suggested, potential risk factors for development of PI have never been examined. Therefore, this study aimed to identify characteristics that may be associated with PI development in lung transplant recipients.

Methods: We retrospectively identified 13 cases of PI occurring post-transplant between 2013-2021. Chart review was conducted to collect variables including demographics and PI clinical characteristics for the patients. Pre-, intra-, and post-operative events for 12 patients were also collected (excluding 1 patient who was transplanted at an outside institution). Descriptive statistics were used for analysis.

Results: The incidence of PI at our institution was 2.3% (12/523). Mean age of patients presenting with PI was 55.2 years, though all but one (20 years old) patients were older than 50. The most common indication for transplantation was interstitial lung disease (61.5%). On average PI occurred 417.3 days post-transplant, though cases occurred from 5 days to 4 years post-transplant, with 4 occurring >1 year after transplant. At the time of PI diagnosis, 5 patients were being treated with “pulse dose” steroids for rejection, and eight were on the second-line drug mycophenolic acid instead of mycophenolate moftel. Three patients underwent negative exploratory laparotomy. Survival at 1 month after PI was 92.3%, with one patient dying 38 days post-retransplantation from primary graft dysfunction complicated by sepsis and multiorgan failure with PI noted on imaging. Recurrences occurred in 2 patients, with one patient having three recurrences up to 5 years post-transplant. Nine of 12 patients had elevated pulmonary artery pressure (PAP) at transplantation, with an average systolic pressure of 55.3.

Conclusion: We characterize the clinical characteristics of pneumatosis intestinals in 13 lung transplant recipients at our institution. Our findings suggest that PI develops in older patients who had elevated pre-transplant PAP. Furthermore, more than half of the patients with PI were on 2nd-line immunosuppression suggesting predisposition to gastrointestinal issues. Additionally, a significant fraction was on high dose steroids at the time of PI diagnosis, corroborating the findings in the literature of association between aggressive immunosuppression and PI. Similar to published studies, most post-transplant PI cases were benign and surgical intervention was potentially unnecessary. More rigorous studies on risk factors for PI in transplant recipients are warranted.
The Dynamic of Physical Capacity and Quality of Life in Recipients After Heart Transplantation

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Objective: to estimate the dynamic of physical capacity (PC) and quality of life (QoL) in recipients after heart transplantation (HTx).

Methods: We analyzed the data collected from January 2010 to December 2019 where 131 heart transplant patients (mean age - 47.1±13.5 year-old; 100 – male) were included. Recipients performed cardiopulmonary exercise test (CPET) before, 3 months, 1 and 3 years after HTx. Dynamics of VO2peak and ventilatory efficiency (VE/VCO2slope) were measured. Physical activity (PA) was defined by IPAQ questionnaire. We estimated the dynamic of physical capacity (PCS) and mental component summary (MCS) by SF-36 questionnaire.

Results: In 3 months PC significantly increased (VO2peak – 15.6±0.5 ml/min/ kg, p<0.001; VO2pred – 53.8±1.7, p<0.001) and VE/VCO2slope decreased (38.2±1.1, p<0.004). Following 1 year after HTx level of PC continued improving (VO2peak – 18.5±0.5 ml/min/kg, p<0.001; VO2pred – 66.3±2.1, p<0.001; VE/VCO2slope – 36.3±0.9, p=0.148) and results remain stable in 3 years (VO2peak – 18.7±0.5, p=0.130; VO2pred – 67.9±1.9, p<0.001; VE/VCO2slope – 36.8±0.9, p=0.017). According to IPAQ results, less than half of patients were physically active (3 months after HTx – 39% (n=45 from 115); 1 year – 46% (n=50 from 109); 3 years – 48% (n=34 from 71), others preferred a sedentary lifestyle. Three months after HTx 58% reached normal values of PC, in 1 year – 68% and in 3 years – 66%. Physically active recipients showed better results of VO2peak than those who had sedentary lifestyle (3 months – 17.0±0.8 vs. 15.2±0.5, p=0.032; 1 year – 19.4±0.8 vs. 16.9±0.4, p<0.001). PCS also increased (3 months – 41.4±1.1, p<0.001; 1 year – 46.6±1.0, p<0.001) and in 3 years remained stable (46.6±1.0, p=0.882). At the same time in 3 months after HTx MCS improved (48.1±0.9, p=0.001) but then started to slowly decrease (1 year – 46.7±0.8, p=0.004; 3 years – 45.4±0.8, p=0.117). We found correlations between age and CPET results (VO2peak – 3 months (r=0.460, p<0.001), 3 years (r=0.320, p=0.011); VE/VCO2slope – 3 months (r=0.419, p=0.001), 1 year (r=0.381, p=0.001), 3 years (r=0.355, p=0.005)) and PCS (3 months – r=0.391, p<0.001; 1 year – r=0.341, p=0.001; 1 year – r=0.363, p=0.002). There were correlations between VO2peak and donors’ age (1 year – r=0.318, p=0.006; 3 years - r=0.337, p=0.008) and PA (1 year – r=0.315, p=0.006; 3 years - r=0.337, p=0.008). The levels of PCS correlated with VO2peak (3 months - r=0.366, p=0.005; 1 year – r=0.397, p<0.001; 3 years – r=0.361, p=0.006) and with VE/VCO2slope (1 year – r=0.441, p<0.001; 3 years – r=0.378, p=0.004).

Conclusion: All heart transplant recipients improved their physical capacity and quality of life and remained levels of them stable long-term after HTx. Physically active patients showed better results while the older donor and/or recipient’s age are negative factors in reaching normal values of VO2peak.

Chimerism and Bidirectional Alloresponses in Patients Receiving Lung Transplantation

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Introduction: Long-term outcomes after lung transplantation (LuTx) are suboptimal, with 5-year survival < 60%. Graft rejection is a major complication limiting success. Our data suggest that cellular and clonal repertoire changes may have already happened in lung allografts when histology is not diagnostic of rejection. The association among the dynamic replacement of T cell clones in lung allografts, differences of donor graft lymphoid cell load, and eventually help predict graft outcomes and develop novel strategies to promote tolerance after LuTx.
Abstracts

337.10

Monotherapy With TNX-1500, a Fe-Modified Anti-CD154mAb, Prolongs Cardiac Allograft Survival in Cynomolgus Monkeys

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Purpose:
Blockade of the CD40/CD154 T cell costimulation pathway is a promising approach to replace conventional clinical immunosuppressive therapy. TNX-1500 (TNX) is a novel humanized anti-CD154 mAb that contains the hu5c8 Fab region and an Fc region engineered to modulate FcγR2 binding to reduce the risk of thromboembolic events seen with hu5c8 IgG1 in previous clinical trials. Its efficacy was evaluated in cynomolgus monkey heterotopic heart allograft recipients.

Methods:
Cynomolgus monkey heterotopic cardiac allograft recipients were treated with TNX 30mg/kg iv 2x weekly for 2 weeks, then either a ‘standard-dose’ regimen of 20mg/kg weekly from days 21-180 (sTNX, n=5) or a reduced-dose TNX maintenance regimen (10 mg/kg weekly x6, then 20mg/kg monthly; loTNX), with (loTNX+MMF, n=4) or without mycophenolate mofetil (MMF) at 200mg/d po (loTNX, n=4). In 3 sTNX animals therapy was discontinued on day 175. Results were compared to historical data with hu5c8 monotherapy dosed as for loTNX (n=5). Biopsies or explanted hearts were evaluated at three protocol-defined time-points (d45, d90, d180), at earlier explant.

Results:
sTNX (MST >232d, range 116-305) significantly prolonged cardiac allograft survival relative to hu5c8 alone (MST 133d; p=0.016), loTNX (MST 99d; p=0.014), or loTNX+MMF (MST 88d; p=0.011). All grafts treated with loTNX () or with loTNX+MMF () exhibited acute rejection histologically within 90 days, and 7 of 8 grafts failed before day 180. One sTNX graft rejected at 116d in association with bacterial infection; one graft was electively explanted at 181d; and three grafts survived for 57, 90, and 130 days after discontinuing TNX-1500. Neither sustained thrombocytopenia nor micro- or macro-vascular thrombosis were observed. At 90 days, loTNX+MMF had a significantly higher median ISHLT score (2.0) than sTNX grafts (0.2; p=0.016); loTNX+MMF also had a significantly higher median CAV score (1.8) at d90 than either loTNX (0.2; p=0.022) or sTNX (0.3; p=0.026). At subsequent graft explant or end-of-study biopsy (180d), loTNX+MMF had a higher median CAV score (2.4) than loTNX (0.4; p=0.002) or sTNX (0.8; p=0.002). sTNX suppressed the rise in Teff/Tregs ratio at the final time-point (180d or <180d if graft failure) more effectively than loTNX+MMF (3.5 ± 0.9 vs 9.5 ± 6.1, p=0.031). sTNX (5/5) but not loTNX (1/4) or loTNX+MMF (2/4) consistently prevented anti-donor antibody elaboration.

Conclusions:
Blockade of the CD40/CD154 T cell costimulation pathway is a promising approach to replace conventional clinical immunosuppressive therapy. TNX-1500 (TNX) is a novel humanized anti-CD154 mAb that contains the hu5c8 Fab region and an Fc region engineered to modulate FcγR2 binding to reduce the risk of thromboembolic events seen with hu5c8 IgG1 in previous clinical trials. Its efficacy was evaluated in cynomolgus monkey heterotopic heart allograft recipients. Lower TNX maintenance dosing, with or without MMF, was less effective.
Adenovirus-Mediated Adiponectin Gene Transfer in a Rat Model of Orthotopic Left Lung Transplantation

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Introduction: Primary graft dysfunction (PGD) can occur early following lung transplantation (LT) and correlates with acute and chronic lung allograft rejection. Abrupt inflammatory and oxidative stress responses occur within minutes of LT. This ischemia-reperfusion injury (IRI) is believed to be responsible for initiating PGD. Interestingly, adiponectin (APN) a bioactive peptide, has significant anti-inflammatory and cytoprotective properties to pulmonary endothelium and airway epithelium. Thus, gene delivery of APN to donated lungs may decrease the incidence of PGD from IRI. We aim to assess the feasibility and early post-transplant effect of adenovirus-mediated adiponectin gene therapy to donor lungs.

Methods: Male Lewis rats (350-450 g) were randomly allocated into 3 groups (N=5/group), where they underwent in vivo transbronchial instillation of 1) Control: 400 µL of PBS+10% glycerol, 2) Ad-mCherry: adenovirus-mCherry 400 µL of 1.5*1010 PFU, and 3) Ad-APN: adenovirus-adiponectin 400 µL of 1.5*1010 PFU. After 24 h, transduced lungs were procured, flushed with ice-cold low-potassium dextran, and preserved in cold ischemia for ~3 h. Then, left donor lungs were orthotopically transplanted into recipient male Sprague Dawley rats (350-450 g). Following 2 h of reperfusion, blood gas samples were analyzed from the aorta and left pulmonary vein. Finally, recipient rats were euthanized, plasma and lung tissue were collected for wet/dry ratio and further analysis.

Results: Target gene expression in Ad-APN and Ad-mCherry lungs was confirmed using tissue immunofluorescent staining. During the 2 h reperfusion, all recipient rats had stable oxygen saturation (SPO2% >90). The mean arterial partial pressure of oxygen (pO2) for groups 1-3 was 191.0, 193.4, and 231.5 mmHg; the estimated % contribution of donor lung to recipient pO2 was 73.2, 46.0, and 46.5, respectively. On average, wet/dry ratio of left donor lung was 8.7 for Control, 9.5 for Ad-mCherry, and 6.7 for the Ad-APN group. Plasma multiplex cytokine assay showed elevated levels of pro-inflammatory cytokines: IL-6, IL-1β, and IL-18 in Ad-mCherry compared to Control and Ad-APN. Monocyte chemoattractant protein (MCP-1) secretion was significantly higher in the Ad-mCherry group than APN (p = 0.02).

Conclusion: Adenovirus treated lungs with Ad-mCherry, and Ad-APN exhibited comparable lung function post-transplant. Of interest, APN expression modulated the vector-induced inflammation in the Ad-APN group. Furthermore, APN induced the downregulation of MCP-1 secretion by alveolar macrophages. This will impair the chemoattraction of recipient monocytes and neutrophils, therefore potentially attenuating lung allograft inflammation and IRI post transplantation.
337.12

The Use of ECMO in Lung Transplant and hybrid Cannulation: 10 Years of a Single Center Experience

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Introduction: The use of perioperative Extracorporeal Membrane Oxygenation (ECMO) in lung transplantation (LTx) has increased along the years, with multiple well established indications and benefits. In this study, we aim to report the use of intraoperative ECMO at our institution and the employment of hybrid cannulation (femoral vein-aorta configuration).

Methods: Retrospective study at a single center (Instituto do Coração - HCFMUSP, Brazil). The data collection used the REDCap database regarding LTx from 2011 to 2021.

Results: It was performed 291 LTx from 2011 to 2021 and 25 (8.6%) utilized intraoperative ECMO support. ECMO support as Bridge to LTx was used in 5 cases and extended to intraoperative support. Programmed ECMO was used in 10 patients. Central VA cannulation was implemented in 6 patients; 4 patients underwent hybrid cannulation; 4 patients on peripheral VA-ECMO and 1 on peripheral VV-ECMO. In the group of patients on central ECMO, 4 were successfully decanullated. In the hybrid cannulation group, all the patients were successfully decanullated at the end of LTx. The mean time of central cannulation was 7.2 days and 11.2 days in the hybrid cannulation group. When LTx occurred using central VA-ECMO, the mean Intensive Care Unit (ICU) stay was 23.3 days and 34 days when hybrid cannulation was used. The total hospital stay was 41.5 on central ECMO and 52.7 on hybrid cannulation.

Conclusion: Intraoperative ECMO support is well established on LTx, despite the low rate of utilization at our center. The use of hybrid cannulation may offer an alternative when supporting acute patients with less central manipulation and allowing more easily the transition to VV-ECMO at the end of LTx when required.

340.1

Liver Cirrhosis and Fibrosis in the Post-kidney Transplant Population: Misdiagnosis of Fibroscan Assessment

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Introduction: There is an increased use of hepatitis C positive donors to negative recipients in organ transplantation, with special interest in the Kidney transplant (KT) population. Patients are assessed for liver cirrhosis and fibrosis prior to listing for KT. We report here a case series of 20 patients submitted to robotic-assisted cholecystectomies post-KT with incidental intra-operative finding of liver cirrhosis not previously known.

Methods: Prospectively collected data of patients submitted to robotic-assisted cholecystectomies at the Jackson Memorial Hospital, University of Miami, Miami Transplant Institute, in the period of Aug-2021 to Mar-2022, during the first phase of implantation of the Transplant Robotic Program. Data relative to the pre-operative, intra-operative and post-operative periods were collected, including clinic-demographic characteristic of the patients, surgical metrics, and pathology findings. Continuous variables were analyzed with Student t-test, categorical variables were analyzed with chi-square test. A p-value of less than 0.05 was considered to be statistically significant.

Results: 16 patients were included, of those 10 (62.5%) were male. The median age was 57 years old (IQR 50-77.8). Of all cases analyzed, 10 (62.5%) were indicated for surgery based on symptomatic cholelithiasis only, without preoperative radiologic signs of chronic or acute cholecystitis. None of the patients had previously known liver fibrosis or cirrhosis per fibroscan assessment. The median intra-operative robotic console time was 30 (IQR 23-49) min. Intra-operatively, 10 (62.5%) patients were found to have macroscopic liver fibrosis/cirrhosis, 8 (50%) had chronic cholecystitis, and 4 (25%) had acute cholecystitis. The median length of stay was 0.93 (IQR 0.9-1.1) days. There were no postoperative readmissions or complications associated to the procedure.

Conclusion: Liver fibrosis/cirrhosis can be underdiagnosed with fibroscan assessment, and special careful attention should be dedicated to patients undergoing hepatitis positive to negative organ transplantation.
HLA-C Mismatching Improves Outcomes Following Lung Transplantation

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Introduction: The major barriers to transplant success are polymorphic human leukocyte antigens (HLA) that divide into class I (HLA-A, B, C) and class II (HLA-DR, DP, DQ) molecules. HLA-A and HLA-B molecules are known as the principal ligands for CD8+ T cells, whereas HLA-C molecules are better known as ligands for Killer cell Immunoglobulin-like Receptors (KIR), which control the function of Natural Killer (NK) cells. HLA-C molecules are designated as “C1” or “C2” ligands based on their ability to interact with KIR2DL2/L3, or KIR2DL1, respectively. Historically, HLA-C has been overlooked as a determinant of matching lung transplant (LTX) donors with a suitable recipient. Here, we aimed to determine if donor/recipient mismatches in the amino acid level (called eplet mismatching (epMM)) to stratify patients in low, moderate or high epMM (n=103-104 per group).

Results: Recipients homozygous for HLA-C2 (C2/C2, n=42) had significantly less CLAD than C1/C1 (n=113) or C1/C2 heterozygous recipients (n=130) (p<0.05). Strikingly, the incidence of CLAD was further reduced in C2/C2 recipients that received a completely mismatched C1/C1 allograft (n=14), compared to receiving a completely matched allograft (n=8) or an allograft from a heterozygous donor (n=20). Indeed, ~80% of completely mismatched HLA-C LTX recipients remained CLAD-free for up to 10 years post LTX. Moreover, donors and recipients that had higher epMM across HLA-C had significantly less CLAD (p<0.05), an observation that was not explained by linkage disequilibrium with other HLA molecules.

Conclusion: Our data implicates a role for HLA-C in the development of CLAD. Contrary to the principles that govern alloreactive T and B cell responses, HLA-C mismatching was not detrimental to LTX outcome, but potentially beneficial, representing a paradigm shift in assessing donor-recipient compatibility at the amino acid level (called eplet mismatching (epMM)) to stratify patients in low, moderate or high epMM (n=103-104 per group).

Comparison of HLA Compatibility Algorithms to Predict Longterm Survival and CLAD Following Lung Transplantation

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Introduction: Outcomes following lung transplantation (LTX) remain poor, despite recent advances in sequencing technology and the development of multiple algorithms defining immunological compatibility between recipient and donor. No consensus has been achieved regarding the best approach to define HLA compatibility in LTX. Here, we compared numerous available HLA compatibility approaches, including T- and B-cell epitopes, electrostatic charge and amino acid mismatching, using a high resolution typed, well characterised cohort, to determine which approach best predicts outcomes following LTX.

Methods: In this retrospective single-center study, 277 donor-recipient transplant pairs were retrospectively HLA typed by Next generation sequencing (NGS) for all HLA loci. (HLA-A-DPA). HLA mismatching was defined using HLAImmatchmaker eplets (epMM), HLA-EMMA epitopes (EMMA), PIRCHE T-cell epitopes (PIRCE), electrostatic differences (EMS) and amino Acid mismatches (AAMM). Associations with mismatching scores generated by the different algorithms with CLAD (BOS/RAS) and overall survival were calculated using adjusted cox proportional modelling and Kaplan-Meier survival curves to demonstrate time to outcomes (SPSS v.21).

Results: Lower HLA-class II compatibility was associated with increased overall survival for all algorithms, with lower HLA-DR, -DQ and -DOA mismatches generated by PIRCE and epMM independently associated with increased survival. Lower HLA-DR compatibility was significantly associated with increased time to RAS for all algorithms. Lower epMM and PIRCE HLA-DOA was also associated with increased time to RAS, however the algorithms that did not separate DOA and DQB, did not reach significance.

Conclusion: Lower class II mismatching, specifically for HLA-DR and DO, for all approaches associated with improved graft and patient survival. The PIRCE and HLAMatchmaker algorithms that separate compatibility based on individual alleles/chains provide a higher degree of granularity, which may be useful to select the best matched recipient. Regardless, reducing the level of HLA mismatching, in either T- or B-cell epitopes, electrostatic differences or amino acid would improve outcomes following LTX and potentially guide immunosuppression strategies.

### Results Table

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### P-values

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Longitudine Foundation.
Accessibility to the Kidney Transplantation Beyond Immunology

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Background: Kidney transplantation (KT) has proven to be the preferable kidney replacement therapy (KRT) as it provides a better survival and quality of life. Well-known patient-related factors influencing patients’ access to KT are blood type, age, comorbidities, and pre-sensitization to HLA antigens. Research on home dialysis modalities’ effect on this matter is scarce.

Methods: We included all adult patients who started kidney replacement therapy (KRT) between 2004 and 2017 in the Helsinki University Hospital treated with home dialysis modalities (N=536), including home hemodialysis (HHD) and peritoneal dialysis; both CAPD and APD. A control group of in-center HD (ICH) patients was randomly selected (N=200). The patients were followed-up until kidney transplantation, death, or end of follow-up in December 2020. We retrieved from registries variables with a potential effect on access to transplantation, of special interest we considered dialysis modality at 90 days after initiating KRT.

Results: In all, 481 out of 736 patients were waitlisted for kidney transplantation, of whom 423 were transplanted (88%), 23 patients (5%) died on the waitlist (WL), 24 were permanently removed from the WL (5%) and 11 were still on the WL at the end of FU. The probability of waitlisting was 2.1 as high in CAPD patients (p=0.004), and 7.9 times as high in both APD and HHD patients (p<0.001) compared to ICHD. Cardiovascular morbidity did not affect waitlisting. Of those who were waitlisted, both ICHD (N=74) and CAPD (N=80) patients were older than APD (N=199) and HHD (N=128) patients (mean age 54; 56; 48 and 49 YO respectively). Mean (95% CI) time elapsed from KRT initiation to WL inclusion was 307 days (251-362), time from WL to KT was 458 days (542-636) and time off the WL due to an intercurrence was 96 days (80-112). There were no differences between dialysis modalities in terms of time from WL to KT (p=0.176), but time to WL was significantly longer in ICHD patients (p=0.014) (Figure 1) The time off the WL equally delayed KT irrespective of the dialysis mode. (p=0.141)

Dialysis modalities had an impact on the time elapsed from WL to KT (log rank p=0.028). By Cox regression analysis the variables that were significantly related with the outcome were panel reactive antibodies type 1 (p=0.033), and time off the WL (p<0.001), while cardiovascular comorbidity (p=0.246), dialysis modality (p=0.208), malignancy (p=0.675), panel reactive antibodies type 2 (p=0.679) and age (p=0.054) did not reach the level of significance. Altogether 732 episodes resulted in the patients being temporarily removed from the WL, and the most common reasons were PD-peritonitis (20%), other infections (26%), and surgery/dental treatment (10%). On the other hand, both vascular access complications (1%) and cardiovascular intercurrences (4.9%) were uncommon.

Conclusions: Dialysis modality significantly influences patients’ access to transplantation. APD and HHD modalities provided a benefit in terms of accessing the WL. In patients wait listed, intercurrent complications during dialysis, mainly infections, significantly prolonged the waiting time for KT in all patients beyond immunological reasons.
Factors Influencing Access to Kidney Transplantation (FIAT): An Integrative Multiphasic Stakeholders’ Perspective

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Introduction: Kidney transplantation is considered the optimal form of renal replacement therapy. However, in the Netherlands, about sixty percent of patients on dialysis are not actively considered for transplantation, which is difficult to explain based on basic medical variables only. Indeed, various (non-)medical barriers to optimal access to transplantation have been mentioned in literature. Remarkably, no systematic inventory exists on these multiple (non-)medical barriers and the different perspectives on these barriers by these multiple stakeholders’ perspectives. Hence, the present qualitative study presents the various (non-)medical barriers to optimal access to transplantation from different perspectives of multiple stakeholders.

Method: Stakeholders involved in renal care are interviewed in two different phases about attitudes (phase 1) and integrative perspective of the different stakeholders (phase 2) regarding barriers to optimal access to transplantation. The topic list for the interviews contains six themes: psychological, policy, medical, ethical, social, and economic. The interview method followed grounded theory principles.

Results: A total of 117 participants were involved: patients (21), donors (10), social workers (25), nephrologists (22), surgeons (5), nurses (6), policy officers (24) and representatives of insurance companies (4). The following major barriers are typical for the six themes:

1. Psychological: Fear for transplantation relates to delay kidney transplantation;
2. Policy-based: Health care providers experience a lack of or unclarity regarding treatment guidelines;
3. Medical: No consensus on criteria for acceptance for transplantation, e.g., age, BMI, comorbidity;
4. Ethical: Lack or insufficient use of programs/interventions that could help patients reach equal access to transplantation;
5. Social: Lack of an effective social network or lack of skills to activate social support system;
6. Economic: Differences in purchasing agreements and following reimbursements for dialysis and transplantation could provide an economic incentive for choosing one or the other therapy.

Conclusion: According to participants, access to transplantation rely heavily on a well-informed and acting patients, donors and health professionals. Despite the existence of national clinical guidelines, participants report ambiguity about their existence. Decision making by patients and donors is hampered by a lack of information about the different options, fears and difficulty to the complex decision-making process with multiple stakeholders. Financial incentives can influence access as they are not always aimed at encouraging early referral to kidney transplantation. Stakeholders state that access to kidney transplantation could be improved when these issues would be addressed. Next to the results of phase 1, the results of phase 2 (integrative perspective of stakeholders) will be presented.

Variability in Workup and Eligibility Criteria for Adult Kidney Transplantation Among Canadian Transplant Centres

Faisal Tallaa1, Lakshman Gunaratnam2, Marcelo Cantarovich1, Hélène Cardinal2, Stephanie Hoar4, Olwyn Johnston5, Martin Karpsinska5, Tammy Keough-Ryan2, Joseph Kim4, Caroline Lamarche4, Khaled Lofti5, Jeff Ma13, Rahul Mainra11, Mélanie Masso12, Shaifali Sandal1, M. Khaled Samseeddin13, Kevin Wen14, Rita S. Suri1.
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Introduction: All potential kidney transplant recipients undergo rigorous evaluation to rule out or ensure appropriate treatment of conditions that may increase risk of post-transplant complications, but specific recommendations regarding workup and kidney transplant candidacy vary across published guidelines. We assessed current pre-transplant evaluation practices and eligibility criteria for adult kidney transplantation across Canada to elucidate differences in guideline interpretation and identify areas of most uncertainty.

Methods: We compared published guidelines on kidney transplant workup and eligibility in order to create a focused digital survey that included both undisputed and controversial domains. The survey was divided into: referral process, history/physical exam, multidisciplinary assessments, laboratory/imaging, and contraindications. Given the many cancers and different staging for each, malignancy-related inquiries were simplified. The medical directors of all 18 Canadian adult kidney transplant programs were invited to complete the survey. We defined consensus and uncertainty, respectively, as >90% and <65% agreement between centers.

Results: Survey completion rate was 78% (14/18). There was consensus on mandatory pre-transplant viral serology testing, tuberculosis screening, and dental evaluation, while cardiac evaluation protocols varied considerably. Of 28 questioned conditions, 6 were considered absolute contraindications by >90% of centers (active bacterial infection/malignancy, non-healing ulcer, COVID-19, severe lung/liver disease). Moderate uncertainty existed for: medication non-adherence (57%), symptomatic heart failure (50%), recent myocardial infarction (57%), and frailty (35%). Other parameters demonstrating wide variability included latent tuberculosis treatment protocols, and exclusion thresholds for parathyroid hormone, body mass index, left ventricular ejection fraction, and blood pressure. Centers used several guidelines to determine eligibility for patients with treated cancer.

Conclusion: There is marked variability in evaluation requirements and eligibility criteria for kidney transplantation across Canada. National harmonization of evaluation processes and eligibility criteria may help to ensure more equitable and transparent access to kidney transplantation for Canadian patients with end-stage kidney disease.
Prehabilitation of Candidates for Renal Transplantation (PreCareTx): A hybrid Study

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Introduction: It is important for kidney transplant candidates (KTCs) to be in an optimal physical and psychological state prior to kidney transplantation. This is because the patient must be able to handle the stress of the upcoming surgery and withstand post-operative recovery time. However, the health status of KTCs is often compromised due to disease progression, comorbidities, and the adverse effects of dialysis - and is associated with impaired physical fitness, an increased risk of psychological problems, and a lower quality of life. The aforementioned problems are encapsulated within frailty. “Prehabilitation” is an intervention that modulates frailty and enhances the fitness of a patient prior to an operation. It enables the patient to withstand the stress of surgery and may be an effective way to improve the overall wellbeing of KTCs. Prehabilitation focuses on implementing lifestyle changes with the goal to improve pre- and post-transplant outcomes. It comprises physical training, dietary management, and psychological interventions. A multimodal prehabilitation program for KTCs has not been established so far. The PreCareTx project aims to develop, implement, and test a multimodal prehabilitation program in order to elevate the physical and psychological fitness of KTCs and consequently improve their frailty status.

Main objective: To examine the effectiveness of prehabilitation to improve the physical and psychological fitness of KTCs during the waiting-list period and its potential for further implementation in a real-world situation.

Method: A hybrid study design will be utilized, comprised of a randomized controlled trial to test the effectiveness of prehabilitation to improve the frailty status of KTCs and a mixed-methods study to gather information on its potential for further implementation. One hundred and twenty-eight patients with one or more modifiable problem(s) will be randomized to care as usual or prehabilitation. The prehabilitation program will be tailor-made and multi-modal in nature, consisting of physical exercise, nutritional plans, and psychosocial support. It will span over the course of twelve weeks and patients will be monitored weekly by a lifestyle coach. The primary endpoint will be change in frailty status. Secondary endpoints include changes in physical activity, nutritional status, psychological fitness, quality of life, and clinical outcomes regarding waitlist mortality, delisting, complications, number of hospital admissions assessed by medical record review until transplantation.

Expected results: We hypothesize that, compared to usual care, a prehabilitation program tailored to individual patients’ needs will improve the overall fitness of kidney transplant candidates. Consequently, this may enable them to better withstand the stress of the transplant surgery which could improve post-transplant outcomes.

Effects of Exposure to Sensitizing Factors and Degree of Pre-transplant Sensitization in the Prognosis of Kidney Graft

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Introduction: Renal transplant success is affected by several long-term events; the main cause of graft loss is antibody-mediated rejection. These rejection events will occur more frequently the greater the pre-transplant immunological risk, which depends largely on the presence of anti-HLA antibodies (HLA-Ab) directed at the donor due to previous exposure to sensitizing factors. The impact of natural HLA-Ab (pretransplant HLA-Ab without exposure to sensitizing factors) has not been clarified. A better understanding of the risk groups, would help us to give us guidelines for the management of long-term immunosuppression. The objective of this study was to compare the immunological outcomes and graft survival according to exposure to sensitizing factors and the presence of pre-transplant HLA-Ab in kidney transplant recipients.

Methods: Retrospective study that included transplanted patients between January 2014 and December 2015. Four groups were compared, based on exposure to sensitizing factors and the presence of pre-transplant HLA-Ab. The relevant outcomes to be analyzed between the 4 groups were: generation of long-term immunosuppression. The objective of this study was to compare the immunological outcomes and graft survival according to exposure to sensitizing factors and the presence of pre-transplant HLA-Ab in kidney transplant recipients.

Method: A hybrid study design will be utilized, comprised of a randomized controlled trial to test the effectiveness of prehabilitation to improve the frailty status of KTCs and a mixed-methods study to gather information on its potential for further implementation. One hundred and twenty-eight patients with one or more modifiable problem(s) will be randomized to care as usual or prehabilitation. The prehabilitation program will be tailor-made and multi-modal in nature, consisting of physical exercise, nutritional plans, and psychosocial support. It will span over the course of twelve weeks and patients will be monitored weekly by a lifestyle coach. The primary endpoint will be change in frailty status. Secondary endpoints include changes in physical activity, nutritional status, psychological fitness, quality of life, and clinical outcomes regarding waitlist mortality, delisting, complications, number of hospital admissions assessed by medical record review until transplantation.

Expected results: We hypothesize that, compared to usual care, a prehabilitation program tailored to individual patients’ needs will improve the overall fitness of kidney transplant candidates. Consequently, this may enable them to better withstand the stress of the transplant surgery which could improve post-transplant outcomes.
Analysis of Argentinian HLA Genotypes According To Reference Populations in HaploStats Database, Focus on Donor’s Reported Ancestry and Geographical Distribution

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Introduction: Argentina shows great cultural diversity due to several waves of Colombian and post- Colombian migrations into South America that merged with the ancestral population. The majority of Argentinians are of European descent (South American of European descent, SAE), “mestizo” (mixed European and Amerindian ancestry) and less represented people of Native American descent (South American of Amerindian descent, SAA).

Those migrations, in turn, increased HLA genetic diversity. To date, the admixture observed in Argentinian's genotypes continues to be underspecified. We have previously shown differences in HLA allele frequencies of Umbilical Cord Blood (UCB) units taking into consideration donor’s reported ancestral origins and geographic distribution. Clear differences were observed in allele frequencies between the groups SAE and SAA but also in terms of geographic distribution, being SAA more represented in the North of our country. To further study such differences, we analyzed our samples within the reference populations according to HaploStats web application (http://www.haplostats.org), database that includes HLA haplotype frequency information relative to various global and ethnically specific populations.

Method: High resolution HLA A-C-B-DRB1-DQB1 typing from 451 Cryopreserved UCB units were analyzed using HaploStats (HLA Dataset NMDP full 2011/Unphased Genotypes) for all reference populations (AFA, API, CAU, HIS, NAM) with special interest in SCAHIS. Informed consent was collected from all donating mothers. Ethical approval was provided by the Ethics Committee of the Hospital de Pediatría Garrahan (No. 1109/2018).

Results: Frequencies in some/all reference populations were observed for 420 UCB units. Among the 31 units, which failed to be represented in HaploStats database, 14 (45%) were reported as SAA and 12/14 collected in the North of our country, whereas only 7 (22.6%) were reported as SAE, all collected in the central region of Argentina. The remaining 10 units showed mixed or unknown origins: 2 mixture of both (SAA and SAE), and 8 of other mixed or Unknown origins, 6 of which include some SAA component.

Conclusion: Although HaploStats includes HLA haplotype frequency relative to various global and ethnically specific populations, our results showed that our ethnic minorities are still under-represented. Therefore, further analysis of HLA frequencies will help improve collection policies in the Public Cord Blood Bank to achieve its goal of increasing our patient’s chance to find a compatible graft.

Flow Cytometric Pattern of Gamma Delta TCR Expression Identifies Outcomes in Kidney Transplantation

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1Institute for Computational Health Sciences, UCSF, San Francisco, CA, United States; 2Pediatrics, UCSF, San Francisco, CA, United States; 3The Harker High School, San Jose, CA, United States; 4Surgery, UCSF, San Francisco, CA, United States; 5Kidney Transplant Unit, Nephrology Department, Bellvitge University Hospital, Barcelona university, IDIBELL, Barcelona, Spain.

Purpose: The main challenge with kidney transplantation is the possibility of rejection, classified into two types, antibody-mediated rejection (ABMR) and T cell-mediated rejection (TCMR). The role of γδ T cells in renal transplantation outcomes is yet to be clarified.

Methods: We studied the immune repertoire in the peripheral blood of 25 unique kidney transplant recipients with both TCMR and ABMR and stable (STA) allografts confirmed by renal allograft biopsies. Using RNASeq data on these samples we conducted statistical computational approaches to compute the immunoglobulin and T-cell receptor (TCR) reads from RNA sequencing data. A TCR-based multi-parameter flow cytometry protocol was designed to detect γδ T cells in an independent validation set of AR samples to evaluate the ability to differentiate TCMR from ABMR by a blood sample cytometric analysis, paired with the allograft biopsy.

Results: We found that the ratio of all κ, β TCR by γδ TCR is associated with the transplant outcomes, with the ratio being greater in ABMR and TCMR than in STA. In addition, this ratio is associated with several genes showing enrichment in the organ rejection pathways and classifying the patients into their clinical outcomes. γδ T cell lineage is enriched in STA than rejections. Comparing both the rejections, the γδ T cell lineage is significantly (p=0.0131) lower in ABMR.

Conclusions: The TCR panel, based on the γδT cell antibody by flow cytometry, could be advantageous for the rapid identification of the sub-type of kidney rejection by blood sampling, without the need of an invasive biopsy.
The Beneficial Effect of Renal Transplantation on the Immune Phenotype of T Lymphocytes

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Introduction: Changes which happen on the phenotype of T lymphocytes during chronic kidney disease CKD, include reduction of CD4CD25FoxP3 (Tregs) and increase in CD28null and CD16CD56 (NKs) cells. The same alterations are expected to occur following kidney transplantation. Cytometric analysis was performed at time point T0 (day of transplantation) and, then at T3, T6, T12 (3,6,12 months after transplantation, respectively), to estimate the phenotype of T lymphocytes. Based on this analysis T lymphocyte subtypes studied were: CD4, CD8, CD4CD25null, CD8CD28null, NKs, Tregs.

Results: A remarkable and sustained increase in the population of total lymphocytes, as well as of CD4 [510(331), 764(606), 857(661), p<0.0001], CD8 [290(188), 434(318), 528(312), p<0.0001], NKs [198(152), 126(134), 142(152), p<0.001] and Tregs [21[18], 24[20], 34[26], p<0.001], was noticed at time points T0-T3-T6, respectively. All subpopulations remained stable thereafter, during the time period T6-T12. At time point T0, patients who had been on chronic hemodialysis (HD) (N=64) had significantly reduced numbers of Tregs, compared to those undergoing Pre-emptive transplantation (N=7), p=0.006, and increased number of CD8CD28null cells (p=0.006). Furthermore, Treg population had significantly negative correlation with dialysis vintage, r=-0.5, p=0.004. At time point T12, Treg population had significant correlation with previous HD, delayed graft function (DGF) and administration of ATG, (p=0.02, p=0.004, p=0.04, respectively). CD8CD28null cells had significant correlation only with the presence of positive Panel Reactive Antibody, p=0.04.

Conclusions: The beneficial effect of renal transplantation was prompt and evident mainly in the subpopulations of regulatory T cell and NKs, especially in patients undergoing Pre-emptive transplant, however the detrimental effect of HD on CD8 molecule did not seem to be restored during the 12 month period of follow up.
A Successful Program to Durability of Training Effectiveness For Organ Donation Teams
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Introduction: The effectiveness of organ donation team training in improving organ donation status has been proven in various studies around the world. Today, various training courses are held for organ donation teams in the world. However, according to studies, the impact of training courses decreases with the passage of time. Since 2015, a comprehensive training course called IrOSS (Iran OPU Support System) has been held to train organ donation centers in Iran. The program IrOQS (Iranian OPUs Quality control system) was established to evaluate the durability of the impact of training courses and improve the weaknesses of the centers. In the current study, the impact of IrOQS program after the IrOSS course on PMP of the organ donation centers in Iran was evaluated.

Methods: Totally, 15 donation centers which among 56 country’s centers had a low donation rate were selected and went through IrOSS course. After the training, the IrOQS program was performed seasonally in each center. At each stage of this program, family’s consent rate, donor maintenance, case selection, case detection and brain dead confirmation were evaluated. The weaknesses of the centers were analyzed using the available statistical data. According to the results, solutions were provided and short-term goal-oriented training was also provided. In this study, the PMP of each center before, 3 and 6 months after the IrOSS course and 3 and 6 months after the first stage of IrOQS program and also 3 months after the second stage was calculated and the impact was analyzed.

Results: By going through IrOSS courses, the average PMP of regions increased from 5.62 to 13.33 (Table 1) but after 6 months, it declined to 8.63. At this stage, through the IrOQS program, conditions improved and the average PMP increased to 13.06. 6 months after the evaluation program’s first stage, numbers started to decrease to 9.85 again which then increased significantly to 15.61 by applying the second stage of the program. The results show that the PMP of the target centers increased significantly (P <0.0001) with the implementation of IrOSS and IrOQS programs (Figure 1).

Conclusion: Based on the results, we can say that training the teams from different regions has a significant but temporary impact on organ donation’s improvement whereas by adding consistent evaluation and support, the impact of training becomes consistent and continual.

Table 1. The trends of organ donation (PMP)

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Increasing Organ Donors and Transplants via Interoperability

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Introduction: National regulatory organizations including CMS require that hospitals refer all potential organ and tissue donors to an Organ Procurement Organization (OPO). To replace the current time-consuming and error-prone telephonic referral process, secure, direct, electronic donor referral interfaces are pursued and launched across the country, including automated donor referral triggers to ensure referrals not be missed and be made in a time-sensitive fashion. The goals of implementation are to 1) increase the number and timeliness of referrals (and thus transplantable organs); and 2) reduce Hospital and OPO resource costs.

Method: The secure technical interface ("iReferral") directly connects the OPO and Hospital systems and is accompanied by seamless donor referral triggers within the Hospital EMR. These triggers automatically prompt delivery of electronic donor referrals from the Hospital to the OPO upon pre-determined clinical triggers in the EMR, greatly reducing the need for decision-making and donation knowledge by the hospital staff. An additional trigger option allows staff to “one click” electronically refer for cases such as end-of-life discussions. Immediately the OPO receives a new referral auto populated with actionable patient information and real-time notifications alert OPO staff. The interface automatically returns the associated OPO referral ID number to the patient’s EMR to provide confirmation to the referring clinician. This interface is currently implemented at 50 hospitals across the country, with hundreds more forthcoming.

Results: At a pilot hospital, annualized data after the first year of implementation demonstrated 49% increase in vented referrals and 78% increase in organs transplanted. At another hospital network including 18 facilities, within the first four months of launch there was a 38% increase in vented referrals and an estimated 333 hours of nursing time saved. This same hospital annualized data directly from the EMR, allowing them to mobilize and ultimately recover organs and tissue which likely would have otherwise timed out.

Conclusion: This interface has met the goals of the project to 1) increase the number and timeliness of referrals (and thus transplantable organs); and 2) reduce Hospital and OPO resource costs. Carefully tuned automatic donor referral triggers directly address known challenges with busy and/or telephonic referral process, secure, direct, electronic donor referral interfaces are pursued and launched across the country, including automated donor referral triggers to ensure referrals not be missed and be made in a time-sensitive fashion. The goals of implementation are to 1) increase the number and timeliness of referrals (and thus transplantable organs); and 2) reduce Hospital and OPO resource costs.

Uncovering Work-Related Problems Among Organ Donation Coordinators: The BRiC Research Program

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Introduction: Organ Donation Coordinators (OTDCs) play a fundamental role in deceased organ donation processes. However, due to the emotionally challenging and stressful scenarios faced daily, they are commonly affected by work-related issues (e.g., burnout and compassion fatigue), which can lead to increased turnover, reduced quality of healthcare services and negative impact in Organ Donation Organizations performance. Therefore, Canadian Blood Services has partnered with CHEO Research Institute and the organ and tissue donation community to create a research program to study Burnout and Resilience in OTDCs (The BRIC Research Program). The main objectives of the BRIC Research Program are to investigate the incidence and potential causes of work-related issues among OTDCs and to propose innovative ways of dealing with these issues to support teams and decrease turnover of experienced and exceptional OTDCs.

Method: The BRIC Research Program was built using a participatory approach that provides the best evidence possible to help address the specific needs of knowledge users (Organ Donation Organizations and OTDCs). The BRIC started with the development of a core three-phased study: phase 1, we published a scoping review to investigate the available literature on burnout and compassion fatigue among OTDCs; in phase 2, we are using a mixed-methods approach to explore work-related issues among Canadian OTDCs; and in phase 3, informed by phases 1 and 2, we will develop, implement and measure the impact of interventions designed to address work-related issues among OTDCs. In addition to the core three-phased study, we also completed four related projects: (1) a working meeting with representatives from Canadian Organ Donation Organizations; (2) a reflective narrative paper co-authored by Canadian OTDCs discussing their views and experiences with work-related issues; (3) a qualitative study that investigated experiences of OTDCs about compassion fatigue, burnout and resilience; and (4) a qualitative study that explored the perceptions of OTDCs related to their experiences in a Relationship Centred Care workshop.

Results: An overview of the BRIC Research Program can be found in Figure 1. The outputs of this research program since its launching in 2019 include: a scoping review protocol and a final manuscript publication; three publications regarding the additional projects (reflective narrative, and results from both qualitative studies); 2 poster presentations, 4 invited speaker presentations; and 9 grant applications, 2 granted.

Conclusion: The findings from this research program will inform clinical practice through knowledge dissemination activities. As this study has been designed in collaboration with national knowledge disseminators (Canadian Blood Services) and provincial end users (Organ Donation Organizations) it will yield meaningful results that can be readily integrated into strategies to decrease OTDC turnover.

We would like to thank Canadian Blood Services and the Children’s Hospital of Eastern Ontario for their support funding this work. We thank all Canadian Organ Donation Organizations and the Organ and Tissue Donation Coordinators for their support and participation in this work.

Figure 1. The BRIC Research Program Overview
The Experiences of Organ and Tissue Donation Coordinators Participating in a Team Cohesion and Communication Workshop: An Exploratory Descriptive Qualitative Study

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Background: Organ and Tissue Donation Coordinators (OTDCs) work in a highly specific and complex environment that can lead to challenging work-related issues. To address these issues, organ donation organizations need to take preventive measures to improve OTDCs work-related wellbeing. Therefore, this study aimed to (1) investigate OTDC perceptions about communication skills following the intervention. This work highlights the need for future interventions focused on developing effective interventions to mitigate work-related stressors and to prevent burnout and compassion fatigue are needed, and that managers and institutions should lead the development of such interventions. Regarding the workshop, participants recognized that more strategies to help mitigate work-related stressors and increase support of organ donation among both promotoras and mature Latinas. Knowledge of the steps to become an organ donor and belief that donation knowledge and support, and communication confidence (Study 1). Promotoras participating in the first study were then asked to hold at least 2 group conversations about organ donation and donor designation with mature Latinas (Study 2). Fifty-two group discussions were held with 375 attendees. Self-administered, paper-pencil surveys were completed by promotoras and attendees before and after each group discussion. Descriptive statistics, means and standard deviations and counts and percents, were used as appropriate, to categorize the samples. The Paired Sample t-test was used to assess changes in knowledge of and support for organ donation, and confidence discussing donation and promoting donor designation from pre- to post-test.

Results: Increases in knowledge and support were observed from pre- to post-test, however these changes did not reach statistical significance. A statistically significant increase in communication confidence was found (692.1 (pre) to 852.3 (post); p=.01). The module was well-received, with most participants deeming it well-organized, presenting new information, and providing realistic and helpful portrayals of donation conversations (Study 1). The trained promotoras-led group discussion about organ donation resulted in increased support of organ donation among both promotoras and mature Latinas. Knowledge of the steps to become an organ donor and belief that the process is easy to do increased in attendees from pre- to post-test 30.7% and 15.2% respectively (Study 2). Twenty-one attendees (0.06%) submitted completed organ donation registration forms.

Conclusion: Our results described how the mental health and work-related wellbeing of OTDCs are affected daily by their stressful and emotionally challenging role. The workshop and its components were perceived as being valuable and OTDCs reported positive impacts on team cohesiveness and communication skills following the intervention. This work highlights the need for future studies focused on developing effective interventions to mitigate work-related issues among OTDCs.
Hospital Self-Assessment Tool: A Strategy to Improve Hospital Management in Donation and Transplantation


Introduction: The self-assessment tool for Hospital Management in Donation and Transplantation (HAE), is a systematic instrument that allows reaching a state of the situation on Procurement and Transplantation with emphasis on the management and cultural change of Health Personnel in each center. It has the merit of being a numeralizing and directing management tool, it allows the hospital to be classified according to the results and suggests the package of measures to be applied according to the level reached.

Materials and Methods: The HAE evaluates 5 components with 30 questions and reflect the core aspects that have to do with the Hospital Donation process. The responses are numbered and based on the total score we can classify hospital management and its results into 4 levels: insufficient, basic, intermediate and advanced. For each level, a strategic plan for the improvement of that hospital is defined. The HAE was applied in 5 Hospitals whose donation results are externally audited and their results were compared with the result of the self-assessment.

Results: Hospitals with the best donation indicators (BD/million population, BD/deceased in hospital, BD/deceased in ICU) were the ones that scored the best overall in the tool, so we consider that the HAE is useful in discriminating which hospitals will present better results in donation, allows them to be classified and, based on this, generate a package of measures for improvement. We consider that the HAE is a useful input for the National Transplant Organizations and for the hospital transplant coordinator.

Conclusions: The HAE is an original instrument that allows evaluating the intra-hospital work in Donation and Transplantation, numerizes it allowing continuous benchmarking and is a guide for the elaboration of an Annual Operational Plan to improve the donation indicators of the Hospital. Generates recommendations adapted to improve the Level found in the Hospital.

Current Development Strategy of Organ Procurement Organization in China

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Introduction: The total number of organ donation (OD) exceed 5,000 in 2020 in China, accounting for 14.5% of the global deceased OD. Under the supervision of the national health authority, currently there are 118 organ procurement organizations (OPOs) developed in China to manage daily practice of organ donation and procurement for transplantation. This study provides an overview for the development of OPOs in China and challenges facing in the developing phase. Suggestions were summarized, with aims at seeking up-to-date management model & strategies to increase operational efficiency and service quality.

Methods: Characteristic of current Chinese OPOs management mode and key elements of constructing an OPO with high efficiency were summarized by an expert consensus meeting and a survey completed by 72 experts from 21 provinces. Among them, 42% are the leader from hospital/OPO/transplantation department, and 38% are OPO professionals/coordinators, and 11% are medical staff from transplant department. The rest are professionals in the field of ICU and others.

Results: There are 4 OPO management models adopted in China, namely, provincial independent OPO (developed as an independent & unique non-profit organization in a province), provincial OPO (a unique but hospital-affiliated OPO in a province), the transplant hospital-based OPO (there are more than one OPOs in a province), and OPO alliance (the OPO is developed by more than one transplant hospitals together). There are more than one OPO alliance in a province). Results from the survey show that different OPO management models have its pros and cons. In terms of medical resources & facilities, hospital-based OPO is better than the others. On the other hand, provincial independent OPO has stronger advantages on autonomous control in institutional and financial management. Provincial independent OPO model ranks first in the comprehensive competing score, followed by the hospital-based OPO model. By collecting the views of experts on the key elements of constructing an efficient OPO, 20 key elements were identified. The most important three elements are, namely, availability of support of national/local policies for OPO, the creation of effective donation hospitals cooperation network and a well-organized financial management model.

Conclusion: OPOs have been established in China to manage organ donation and procurement activities. The OPO management models & their performance metric vary among provinces. To achieve better results, the number of OPOs needed to be reduced in regions with more than one OPO.
341.9

An Australian Survey on Public Opinion Regarding Death And Organ Donation: Relationship of Demographic Factors To Opinions

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Introduction: In an on-line survey of the Australian general public, support for organ donation (OD) was high (overall >70%). Opinions about death determination appeared to be more aligned with impressions of quality-of-life outcomes than with biologic definitions of death [1, 2]. Nonetheless, consent rates to OD in Australia are around 50%, despite interventions [3]. We analysed our survey to determine demographic factors associated with differences in opinion.

Method: On-line survey of a representative sample of 1017 members of the general Australian public, comprising 3 ICU case scenarios & multiple-choice questions on death definition & OD decisions. Participants’ age, sex, religious affiliation, & educational level were collected.

Results: Respondents matched Australian population demographics; 51% male, median age 52 years (male) & 42 years (female). 76% lived in metropolitan centres & 57% at least tertiary educated. 23% claimed cultural identity other than Australian & 22% spoke other than English at home. 36% claimed no religious affiliation & 58% identified as Christian. Being religious (p<0.001), tertiary educated (p<0.03) & older (p<0.01) were associated with claimed greater knowledge of OD, whereas non-Australian cultural identity was negatively associated (p<0.01). 70% agreed that a patient determined brain dead was ‘dead’, with older respondents more likely to agree (p<0.001) and non-Australian identity less likely (p<0.05). Female respondents were less confident (p<0.001). Support for OD was higher with increasing age (p<0.001) & lower for those with non-Australian identity (p<0.001) & religious affiliation (p<0.01). In a circulatory death scenario, >70% agreed with life-support withdrawal given prognostic factors, with older (p<0.001) respondents more likely & religious respondents less likely (p<0.001) to agree. Religious respondents were less likely to agree that the patient could be declared dead 2 minutes following circulatory standstill (p<0.03). Older respondents were more likely (p<0.001), and religious less likely (p<0.05) to agree to organ procurement even if this were the proximal cause of death. In a ‘first-person consent’ scenario, 61% of respondents agreed that the patient’s wishes to be taken to the operating room for organ procurement prior to death should be honoured. Female (p<0.01) and religious (p<0.001) respondents were less likely to agree.

Conclusions: We found a consistent relationship between age, religion & female sex and opinions about death & decisions regarding OD. These findings could be useful in advancing strategies to promote OD in the community and to close the gap between reported support for OD and the actual level of support as evidenced by family consents at the bedside of the potential cadaveric donor.

References:
Sydney Medical School Foundation.

341.10

Disparity in Access to Kidney Transplantation in the Province of Buenos Aires, Argentina

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Introduction: Kidney Transplantation (KT) is a practice characterized by a high demand for the supply of available kidney grafts. There are certain conditions that affect the accessibility of groups of patients to this treatment. The objective was to evaluate factors of disparity, traditionally recognized, in access to KT in the province of Buenos Aires, Argentina, taking the year 2019 as the analysis period to avoid the effects of the Covid 19 pandemic on it.

Methods: The following variables on accessibility to KT were analyzed: funder, sex, age and cause of Chronic Renal Insufficiency. For the analysis of transplant activity, the indicator Transplants per 100 patients exposed to risk per year was used. For the analysis, the Argentine Registry of Chronic Dialysis 2019 and the National Procurement and Transplant System of the Argentine Republic (SINTRA) were used as data sources.

Results: The mean time (in months) to enter the Waiting List (WL) of patients with Public Subsidy was 14 months compared to 11 months as the mean time of all patients in the Province of Buenos Aires. The average stay in WL from admission to the transplant was 57 months in subsidized patients, while the provincial average was 40 months. Of the total number of KT performed in 2019 on Buenos Aires patients (n= 494), 101 were performed on patients with public subsidies (20%), when it is estimated that 40% of people have public coverage in the province of Buenos Aires. 59% of the transplants (n=292) were performed on men, with women being more frequent donors for their husbands, fathers, brothers and sons. When diabetes was analyzed as a cause of End-Stage Chronic Kidney Disease, it was observed that in patients over 44 years of age, the rate of transplants per 100 patients exposed to risk per year exceeded was 2.6 vs. 5.5 in the other causes. Regarding age, an increase in transplant rates (100 patients exposed to risk per year) was observed in all age groups (including those over 65 years of age) in the last 10 years, being in the year 2019: 0 -19 years: 26.9, 20-44 years: 8.6, 45-64 years: 4.9 and over 65 years: 1.9.

Conclusion: In the Renal Transplant activity in the province of Buenos Aires, a disparity in access was observed for the population with public subsidies compared to the group that has social security coverage. Women were transplanted less than men despite being more active as donors in Renal Transplantation with living donor. Patients with diabetes over 44 years of age have lower transplant rates than kidney patients with other causes, and in all age groups there was an increase in transplant rates, although it decreases as the age increases.
341.11

Online Perspectives of Deemed Consent Organ Donation Legislation in Nova Scotia, Canada: A Thematic and Content Analysis of Commentary in Facebook Groups

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Background: The Canadian province of Nova Scotia recently became the first jurisdiction in North America to implement deemed consent organ donation legislation. Changing the consent models constituted one aspect of a larger provincial program to increase organ and tissue donation and transplantation rates. Deemed consent legislation can be controversial among the public, and public participation is integral to the successful implementation of the program.

Objective: Social media constitutes key spaces where people express opinions and discuss topics, and social media discourse can influence public perceptions. This project examined how the public in Nova Scotia were responding to the legislative changes in Facebook groups.

Methods: This project analyzed 2,337 comments on 26 relevant posts in 12 different public Nova Scotia-based Facebook groups. We conducted thematic and content analysis on the comments to determine how the public was responding to the legislative changes and how the participants interacted with one another in the discussions.

Results: Our thematic analysis revealed principle themes which supported and critiqued the legislation, which raised specific issues, and which reflected on the topic from a neutral perspective. Subthemes showed individuals presenting perspectives through a variety of themes which included compassion, anger, frustration, mistrust, and a range of argumentative tactics. Comments included personal narratives, beliefs about government, altruism, autonomy, misinformation, and reflections on religion and death. Content analysis revealed that Facebook users react to popular comments with “likes” more so than other reactions. Comments with the most reactions included both negative and positive perspectives about the legislation. Personal donation and transplantation success stories as well as attempts to correct misinformation were some of the most “liked” positive comments.

Conclusions: The findings provide key insights into Nova Scotian perspectives on deemed consent legislation as well as organ donation and transplantation broadly. The insights derived from this analysis can contribute to public understanding, policy creation, and public outreach efforts that might take place in other jurisdictions considering the enactment of similar legislation.

The authors thank and acknowledge Health Canada, Genome Canada, Genome Alberta, and the Canadian Institutes for Health Research for their generous support of Legislative Strategies to Improve Deceased Organ Donation in Canada: A Special Focus on Evaluating the Impact of Opt-Out Legislation in Canada LEADDer and Precision Medicine CanPREVENT AMR: Applying Precision Medicine Technologies in Canada to Prevent Antibody Mediated Rejection and Premature Kidney Transplant Loss.

341.12

Sharing Under KAS – What Is the Impact According to KDPI?

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Purpose: The Kidney Allocation System (KAS) implemented in 2014 changed prioritization of highly sensitized patients and other groups impacting sharing. We sought to determine effects on sharing according to Kidney Donor Profile Index (KDPI) across pre- and post-KAS eras.


Results: Since KAS, sharing has increased across all KDPI groups, and is more pronounced with increasing KDPI. Regional utilization more than doubled for KDPI >85% kidneys while local use decreased 30% from ERA 1 to 5 (Table 1). However, a 60% increase in absolute numbers of DDKT across eras resulted in higher local DDKT volume in ERA 5 despite increased sharing. Sharing for calculated panel reactive antibody (cPRA) 99-100% patients increased post-KAS across all groups, but the effect was less pronounced for KDPI >85% (32% increase compared with 71-89% increase for the other 3 KDPI groups). Sharing for high cPRA patients accounted for only 23% of shared kidneys and 8% of DDKT in ERA 5.

Conclusion: KAS increased sharing across all KDPI groups with the largest change occurring in the regional use of KDPI >85% organs. Higher DDKT volumes over time offset any changes in sharing such that local volumes for all KDPI groups increased. Increased sharing for cPRA 99-100% occurred across all KDPI groups, but represents a minority of kidneys shared.
342.1

Comparable Kidney Transplant Outcomes in Selected Patients With a BMI ≥40: A Personalized Medicine Approach To Recipient Selection

Molly Jacobs1, Karanpreet Dhakwal2, David Harriman3, Robert Stratta1, Alan Farney1, Giuseppe Orlando1, Jeffrey Rogers1, Amber Reeves-Daniel3, Colleen Jay1.

Introduction: Kidney transplantation confers a survival benefit compared with dialysis in most studies of obese patients. Yet, many transplant centers decline patients with a body mass index (BMI) ≥40 kg/m2. Our practice relies on computed tomography imaging to evaluate iliac depth and pelvic angle to assess candidacy (see Figure 1). Our aim was to evaluate post-transplant outcomes including survival in patients according to recipient BMI.

Methods: We performed a single-center retrospective review of adult kidney transplant alone recipients comparing BMI ≥40 patients (n=84, BMI =42±2 kg/m2) to a matched BMI <40 cohort (n=84, BMI =28±5 kg/m2). Patients were matched for recipient age, gender, race, presence of diabetes, and donor type (living vs. deceased).

Results: BMI ≥40 patients were on dialysis longer pre-transplant (5.2±3.2 years vs. 4.1±3.5 years, p=0.03) and received lower kidney donor profile index (KDPI) kidneys (40±25% vs. 53±26%, p=0.003) compared to lower BMI patients. There were no significant differences in prevalence of delayed graft function, reoperations, readmissions, wound complications, patient survival, or renal function at 1 year according to serum creatinine and eGFR. Long-term graft survival was higher for BMI ≥40 patients, including after adjusting for KDPI (BMI ≥40: aHR=1.79, 95% CI=1.09-2.9) (see Figure 2). BMI ≥40 patients had similar weight gain and BMI change in the first year post-transplant (delta weight: BMI ≥40 + 2.5±9.1 kg vs. BMI <40 + 3.0±8.0 kg, p=0.74; delta BMI: BMI ≥40 + 0.9±3.3 vs. BMI <40 + 1.1±3.2, p=0.59). BMI ≥40 patients had a higher mean HbA1c level (6.9±1.7% vs. 5.9±1.4%, p=0.003) at one year post-transplant.

Conclusions: Overall patient survival and complications after kidney transplantation were comparable in BMI ≥40 patients compared to a matched cohort with lower BMI with improved long-term graft survival in the obese patients. BMI-based exclusion criteria for kidney transplantation should be reexamined in favor of a more individualized approach.

Figure 3: Kidney Graft Survival by Patient BMI Classification
2A: ALL DKT AND LDKT

342.2

Sodium-Glucose Co-transporter 2 Inhibitors (SGLT2): Short-term Outcome in Diabetic Kidney Transplant Recipients

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Introduction: The idea of using SGLT2i in kidney transplant recipients (KTR) is a legitimate one after the recent encouraging data for their use in other populations. Patient and graft survival are negatively affected by cardiovascular adverse events and the progressive reduction of graft function. KTR may benefit from the positive cardiovascular and renal outcomes of these drugs. Understandably, many transplant nephrologist may refrain from using SGLT2i because of the side effects profile reported with other patients.

Methods: We collected retrospective data from records of KTR with type II diabetes (T2D) or post-transplant diabetes mellitus (PTDM) (n=97) who were receiving SGLT2 agents plus standard of care (SOC) and compared them to similar group of diabetic patients who were only receiving SOC (n=95). The inclusion criteria were KTR > 18 years with stable graft function who were on SGLT2 for at least three months. Patients with type I diabetes were not included.

Results: There was no significant difference in demographic characteristics between the two groups. HbA1c was significantly reduced (-0.67%) in the SGLT2i group [p=0.0001] versus [-0.24%] in the SOC group [p=0.0127]. Despite the initial dip in the estimated glomerular filtration rate (eGFR), there was a persistent and significant improvement towards the end of the year compared to the SOC group [P=0.0356]. We noticed a significant reduction of proteinuria in the study group [p<0.0001]. The body mass index (BMI) was significantly reduced in the SGLT2i group [p<0.0106]. Patients tolerated the drug well without significant adverse effects (UTI, genital infections, DKA, rejection or cardiovascular events).

Conclusion: The use of SGLT2i in managing diabetic patients post kidney transplantation is safe and has better short-term outcomes on renal function with comparable safety compared to standard of care therapy. A longer follow-up is needed to assess the cardiovascular outcome.
342.3

Outcome Analysis of Patients With Genetic Mutations of Complement Regulatory Proteins in Relation to Incidence of Post Renal Transplant Thrombotic Microangiopathy

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Introduction: Thrombotic Microangiopathy is an occlusive disorder of microvasculature characterized by thrombocytopenia, systemic or intrarenal platelet aggregation, thrombus formation and hemolytic anemia caused by fragmentation of erythrocytes due to the disturbed microvasculature. TMA developing after renal transplantation can be categorized into either De novo TMA, developing for the first time without any evidence of the disease before the transplant or recurrent TMA where native kidneys have failed due to TMA and recur after kidney transplantation. The contribution of complement regulatory gene (CRG) mutation to post-transplant Thrombotic Microangiopathy (TMA) in Indian kidney transplant recipients (KTR) is unknown. This is a study to determine the association of CRG on post-transplant TMA and graft failure.

Methods: A Single Centre, Prospective Observational Cohort Study was undertaken in renal transplant recipients. All live and Deceased donor renal allograft recipients who underwent transplantation from 1st December 2019 onwards till 31st December 2020 were recruited and were followed up for 1 year beyond the last enrolment. Genetic testing was performed with MLPA and Clinical exome sequencing.

Results: 78 KTRs with a mean age of 37.09 ± 13.23 years were enrolled. The Native cause of kidney disease in 55 (70.5%) patients was undetermined and 23 (29.5%) had established cause of chronic kidney disease. 58 (74.4%) were males and 20 (25.6%) were females. CRG mutation was seen in 48/78 (61.5%) KTRs. The allele frequency of the CRG mutation was seen in 48/78 (61.53%) of which duplication of CFHR gene was predominantly seen in 40/78 (51.2%) patients. CRG mutation in this cohort was seen more in the younger age group patients. There was no gender predominance for patients with CRG mutation. None of the patients had a mutation for CFH, CFI, CFB, C3, THBD, DGKE genes. One patient had a mutation for the PLG gene. The incidence of post-transplant TMA was seen in 4/78 (5.12%) patients. Mutation related to aHUS was seen in 2 patients. There was no significant difference in serum creatinine levels of patients with or without CRG mutation at the end of 1 year.

Conclusion: The prevalence of CRG mutation in our KTR cohort was high and is associated with post-transplant TMA in 50% of patients with de novo TMA. The graft outcome at the end of 1 year was similar in patients with mutation and those without mutation. This study suggests that the presence of CRG mutation should not preclude renal transplantation in patients with ESRD.

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Inadequate Iodine Intake and Long-term Outcomes After Kidney Transplantation

Yvonne van der Veen¹, Daan Kremer¹, Adrian Post¹, Daan J. Touw², C. Annema³, Casper F.M. Franssen¹, Stephan J.L. Bakker¹. ¹Internal Medicine, section of Nephrology, University Medical Center Groningen, Groningen, Netherlands; ²Clinical Pharmacy and Pharmacology, University Medical Center Groningen, Groningen, Netherlands; ³Health Sciences, section of Nursing Science, University Medical Center Groningen, Groningen, Netherlands.

Objective: There is a great need for identification of novel modifiable factors to decrease the risk of graft failure and premature mortality in kidney transplant recipients (KTR). We hypothesized that inadequate iodine intake may be one of these modifiable factors. Severe iodine deficiency as a public health problem is now largely under control worldwide, thanks to the introduction of iodized salt in the 1920s. However, for KTR, salt intake may be significantly reduced due to a salt-restricted diet both before and after transplantation, potentially also resulting in inadequate intake of iodine. We aimed to investigate the prevalence and potential determinants of inadequate iodine intake among KTR. In addition, we assessed potential repercussions of inadequate iodine intake, by assessing its associations with graft failure and mortality.

Methods: We determined 24h urinary iodine excretion by means of inductively-coupled plasma mass spectrometry in stable outpatient KTR, enrolled in the TransplantLines Food and Nutrition Biobank and Cohort Study. Inadequate iodine intake was defined as a 24-h urinary iodine excretion <150 µg. Dietary intake was assessed using validated 177-item food-frequency questionnaires. We aimed to identify potential determinants of inadequate iodine intake using logistic regression. In addition, we assessed the prospective association of inadequate iodine intake with graft failure and all-cause mortality using uni- and multivariable Cox regression analysis.

Results: In total, we included 668 KTR (43.4% female, age 53 ± 13 years), at 5.7 [IQR: 2.2 to 12.2] years after transplantation. Median 24h urinary iodine excretion was 201 [IQR: 153 to 266] µg, and 154 (23%) KTR had inadequate iodine intake. Low body height, low urinary sodium excretion, and low intake of bread, eggs, and animal protein were identified as key determinants of inadequate iodine intake. Univariable Cox regression analyses showed that inadequate iodine intake was strongly associated with higher risk of graft failure (HR per doubling: 2.16, 95%CI: 1.36 to 3.43, P=0.001) and mortality (HR per doubling: 2.05, 95%CI: 1.46 to 2.89, P=<0.001). These associations remained materially unchanged after adjustment for age, sex, height, weight, eGFR, 24h urinary protein excretion, HLA class II antibodies, energy intake, urinary sodium excretion, and free T3.

Conclusion: Inadequate iodine intake is prevalent among KTR, and its occurrence appears to be strongly related to dietary factors, including salt intake. Inadequate iodine intake was strongly and independently associated with an increased risk for graft failure and all-cause mortality. These results suggest that supplementation of iodine may reduce risks of graft failure and premature mortality among KTR. Interventional trials are necessary to confirm the potential of stimulating dietary iodine intake or iodine supplementation in KTR.
342.5

Risk Stratification for Kidney Transplant Recipients: A Singlecenter Study

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Introduction: To establish an assessment table of acute rejection for kidney recipients from deceased donors (DD) based on random forest algorithm.

Methods: Recipients in our center from January 2015 to October 2020 were included in this study. Length of follow-up was at least half of the year. All the recipients were randomly divided into two cohorts in a 7:3 ratio, including training cohorts and validation cohorts. In the training cohorts, a random forest classification model was established to screen variables that affect acute rejection. Finally, an assessment table was constructed based on the results of random forest and clinical practice. The assessment table was then validated in the validation cohorts.

Results: Totally 1206 recipients were included. 111 recipients developed acute immune rejection within half of the year. The training and test datasets comprised 844 and 362 patients, respectively. In the training set, donor BMI, age gap between donor and recipient, donor age, recipient age, and cold ischemia time were the most important factors for acute rejection. In the training datasets, the acute rejection was 8.0%, 13.5%, and 26.7%, respectively (p<0.05), and the difference was statistically significant. Intermediate-risk and high-risk recipients had a higher rate of DGF and 1-year mortality compared with low-risk recipients (p<0.05). There were no differences in infection rate between the three groups.

Conclusion: 1. Our assessment table was an effective tool to assess an acute immune rejection within half of the year. 2. For intermediate-risk and high-risk recipients, more immunosuppressive agents should be considered under dynamic infection monitoring.

342.6

Clinical Outcomes Among Patients With Autosomal Dominant Polycystic Kidney Disease (ADPKD) Submitted to Kidney Transplant Compared With a Non-adpkd Paired Group: A Propensity Score Matched Cohort Study

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Background: Beyond the kidney function impairment, the autosomal dominant polycystic kidney disease (ADPKD) patients present abnormal kidney volume, impacting the abdominal venous capacity and the sympathetic/parasympathetic control, which would hypothetically affect early outcomes after kidney transplant (KT). Thus, this study aimed to evaluate whether ADPKD is associated with early outcomes after KT, focused on delayed graft function (DGF).

Methods: This single-center cohort study enrolled 245 patients with ADPKD transplanted from a deceased donor between 2013-17. The control group comprised non-diabetic patients transplanted in the same period (n= 2,596). The analyses were provided before and after a 1:2 propensity score matching. The primary outcome was DGF. Logistic regression was performed to evaluate the variables associated with DGF.

Results: In the ADPKD-group, recipients were older (57 vs. 49 years, p=0.001), more frequently female (51% vs. 37%, p<0.001), and candidate for a first KT (98.4% vs. 92.1%, p<0.001). Before matching, the frequency of DGF was significantly lower among ADPKD-group, 52.2% vs. 60.5% (p=0.012), for whom the time in DGF tended to be shorter (2 vs. 6.5 days, p=0.41). In the multivariable model, the variables associated with the probability of DGF were: male recipients (OR=1.25; p=0.01) and male donors (OR=1.39; p<0.001); hemodialysis as RRT previous to the KT (OR= 1.58; p<0.001) and time waiting for the KT (OR=1.06; p<0.001); KDPI (reference [1-35%], OR[35-51%]=1.47, P=0.01; OR[51-80%]=1.82, P<0.001; and OR>85%]=1.83, p<0.001); and cold ischemia time (OR=1.02; p<0.001). The ADPKD tended to reduce the probability of DGF: OR=0.76, P=0.05. There were no differences in the 1-yr rate of death, 2.9% vs. 3.3% (p=0.71), and graft loss, 4.1% vs. 4.8% (p=0.62) for ADPKD and control groups, respectively. However, the graft loss due to thrombosis was more frequent in the ADPKD-group: 50% vs 33%, p=0.02. After the propensity score matching, the frequency of DGF was 52.2% in ADPKD-group vs. 66.5% in the control group (OR=0.84, p=0.27), with no difference in time in DGF. There were also no differences in the 1-yr rate of death, 2.9% vs. 2.7% (P=0.87), and graft loss, 4.1% vs. 5.3% (P=0.47); however, the graft loss due to thrombosis remained more frequent in the ADPKD-group: 50% vs. 34.6%.

Conclusions: There was no association between ADPKD and, however, as before, as well as after matching, ADPKD recipients presented a significantly higher frequency of graft loss due to vascular thrombosis, despite a low frequency of events.
Audit of Posttransplant IgA Nephropathy Treatment Strategies: Single Center Study

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Introduction: IgA nephropathy (IgAN) is the prevalent form of recurrent disease which has negative influence on graft survival in kidney transplant recipients. Recurrence rate varies from 13% to 50% according to the data available. Approaches to the management of such patients are controversial and there are no any certain treatment recommendations for IgAN in kidney grafts to this day.

Methods: A retrospective single-center study, including 42 patients with biopsy-proven IgA nephropathy in kidney transplant, between January 2014 and August 2020, was performed. Treatment strategies were analyzed. 

Results: Allograft IgAN manifestation time was from 1 to 122 month, with an average of 49.59 ± 30.34 month. The main clinical signs were proteinuria and hematuria – 42,86%; proteinuria less than 1.0 g per 24 hours with and without hematuria – 45,24%; proteinuria less than 1.0 g per 24 hours with and without hematuria – 42,86%; isolated hematuria – 9,52%; elevation in serum creatinine – 2,38%.18 42,86% patients were treated with angiotensin converting enzyme inhibitors or angiotensin II receptor blockers and 11 (61,11%) of them have lost their grafts.

Conclusion: Lack of approved management concepts leads to various strategies.

Conclusion: In this single center, retrospective study and others have failed to confirm any such benefit in the kidney transplant population.

Postoperative Statin Therapy Is Not Associated With Reduced Incidence of Venous Thromboembolic Events Following Kidney Transplantation

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Background: Deep vein thrombosis (DVT) or pulmonary embolism (PE), collectively venous thromboembolism (VTE), are common sources of morbidity and mortality following solid organ transplantation. The pleiotropic effects of statin therapy on inflammation and coagulation may reduce the risk of venous thromboembolism. This study evaluated whether statin therapy is associated with decreased venous thromboembolic (VTE) events following kidney transplantation.

Methods: We performed a retrospective analysis of all primary kidney transplants performed between January 2014 and December 2019 at Mayo Clinic Arizona. Patients were divided into two groups depending on sustained statin therapy during the first year following transplantation. Statin exposure was defined as any statin prescribed on admission for KT or upon discharge from KT plus continuous treatment for one year. Recipient and donor clinical and demographic data were collected. The primary outcome was admission for symptomatic VTE events (deep vein thrombosis (DVT) or pulmonary embolism (PE)). Cox regression was used to model overall survival and VTE event-free survival. Fine and Gray’s regression was used to model outcome for VTE while treating death as a competing risk event.

Results: Sustained statin therapy in the first year following transplant was observed in 16.1% (n=223) of 1384 kidney transplants included in the study cohort. The control group of 1161 patients had no statin exposure during the first year following KT. Demographic and perioperative characteristics are presented in Table 1. The overall incidence of VTE events in the year following kidney transplant was 3.8%. VTE occurred in 4.1% of recipients treated with statins and 3.8% of the controls – (hazard ratio [HR] 0.96, 95% confidence interval [95% CI] 0.43, 2.14, P = 0.93) (Table 2). However, there were significant differences between the groups in terms of age, gender and body mass index. Following sensitivity analysis in which cohort matching was performed to account for these differences, there was no difference in VTE event-free survival (HR 0.85, 95% CI 0.43, 1.68, P=0.65) or overall survival (HR 0.54, 95%CI 0.15, 1.94, P= 0.35) between patients treated with statins compared to controls (Figure 3).

Conclusion: In this single center, retrospective investigation, statin therapy in the year following successful kidney transplant was not associated with a reduction in risk of VTE. Although previous investigations have demonstrated ameliorative effects of statin therapy on rejection, VTE, cancer recurrence and vasculopathy following liver, heart and lung transplantation, the current study and others have failed to confirm any such benefit in the kidney transplant population.
Factors Associated With a Higher Need for Antihypertensive Medications at 12- Months Post Renal Transplantation

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Background: Hypertension (HTN) after renal transplantation can be difficult to control and often requires multiple blood pressure (BP) medications. In this study we examined the incidence and risk factors of “difficult to treat HTN” at one year post kidney transplantation at our center.

Method: A single center retrospective study of renal transplant recipients who underwent kidney transplantation between January 2017 and May 2020 with 12 months follow up. We reviewed patients’ demographics, results of pretransplant cardiovascular imaging, and the change of cardiovascular risk factors during the first-year post kidney transplantation. We divided patients according to the number of their blood pressure medications at one year into two groups; those who required none or one, and those who required two or more medications. We labeled those who required ≥2 as “difficult to treat hypertension”. The target BP during the time of this retrospective study was <140/90mm Hg as per the published guidelines during the time of the study1.

Results: A total of 278 renal transplant recipients were included. The majority (74%) was ≥ 30 years, 58% were men and 80% were living-donor kidney recipients. Preemptive transplantation was 10.1%. PD and HD were 11.5% and 78.4%, respectively. At one year, 70.1% of the patients attained to the target BP goal. Of the total study population; (N: 105, 38%) required ≥ 2 BP medications (i.e., “difficult to treat HTN”). Factors related to a higher need for antihypertensive medications included age (50 vs. 39 years, P<0.001), prior history of hypertension (P=0.006), prior AV fistula vs. dialysis catheter (P=0.044) and diabetes mellitus (P<0.001). Dialysis vintage (including preemptive transplantation), type of dialysis (HD vs. PD), type of transplant (living donor kidney transplant vs deceased donor kidney transplant), and smoking were not different among the two groups. Patients with “difficult to treat HTN” at one year were more likely to have abnormal pre-transplant cardiovascular baseline imaging including abnormal ejection fraction <55% (P=0.044), abnormal wall motion on echocardiography (P=0.004), abnormal perfusion stress test (P<0.001), higher calcium scoring (P=0.002), abnormal cardiac catheterization (P<0.001), and a higher degree of calcifications on CT of pelvic arteries (P=0.006). Patients with “difficult to treat HTN” at one year were likely to have a higher BMI at 12 months (P=0.028) whereas rejection, change of creatinine, weight gain, persistent hyperparathyroidism or anemia at 12 months were not different among the two groups. Multivariate analysis of requiring ≥1 BP medication indicated a relation with age (aOR: 1.025, CI: 1.003-1.048, P=0.026); male vs. female (aOR: 2.413, CI 1.358-4.288, P=0.003); DM (aOR: 2.07, CI: 1.081-3.964, P=0.028); HTN (aOR 2.586, CI: 1.104-6.06, P=0.029). However, the odds ratio for BMI at 12 months was insignificant (aOR: 0.999, CI 0.948-1.053, P=0.98).

Conclusion: At one year post transplantation, about two thirds of our renal transplant recipients required no or only one BP medication. Those who required multiple medications were more likely to be older, males, diabetic, or previously hypertensive. Recipients with abnormal baseline pre-transplant cardiovascular imaging were also more likely to require more medications.

**342.10**

**IgA Nephropathy and Kidney Transplantation According to the Oxford Classification**

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**Introduction:** IgA nephropathy (IgAN) is the most common glomerular disease globally, and its susceptibility and the risk for the development of end-stage kidney disease are related to genetic and environmental factors. IgAN recurrence after kidney transplantation is relatively common, impacting graft function and survival. This study evaluated the risk factors and the clinical, laboratory, and histological characteristics of post-transplant IgAN recurrence, considering the Oxford classification.

**Methods:** Retrospective single-center cohort study including kidney transplant recipients with biopsy-proven IgAN pre transplantation, with analysis of risk factors, clinical, laboratory, and histological characteristics of the IgAN recurrence cases.

**Results:** 53 fulfill the inclusion criteria and were included in the study. Majority was male, white, eutrophic, with a mean age of 27 ± 9 years at diagnosis of IgAN. Systemic arterial hypertension and proteinuria were frequent in the pretransplant period. Four recipients (7.5%) presented IgAN recurrence in a period of 6 to 122 months posttransplant. According to the Oxford classification, they had high scores in the native kidney biopsies, and there was mesangial hypercellularity in all analyzed graft biopsies. None of these patients had received induction immunosuppressive therapy, and all of them presented graft failure in the follow-up.

**Conclusions:** In this series, despite the lower incidence of recurrence of IgAN posttransplant compared to previous reports, progression to graft loss was of 100%.

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**343.1**

**Donor Hypertension Is Associated With an Increased Risk of Early Pancreas Allograft Failure**

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**Background:** About 10% of pancreas allografts are still lost prematurely, despite identification of numerous thrombosis risk factors. We investigated for potential other undescribed risk factors for early pancreas failure.

**Methods:** We conducted a multicentric study including 899 pancreas transplantations between 2000 and 2018. Early pancreas failure, long term pancreas survival, kidney and patient survival were analyzed depending on multiple donor, recipient and perioperative transplantation characteristics using a multivariable cause-specific Cox models stratified on transplant centers.

**Results:** Donor hypertension and donor BMI were significatively associated with an increased risk of early pancreas lost (respectively: HR = 2.43, 95% CI from 1.32 to 4.49 and HR = 1.38, 95% CI from 1.13 to 1.68) and thus of impaired long-term pancreas survival (HR = 1.88, 95% CI from 1.13 to 3.12 and HR = 1.21, 95% CI from 1.04 to 1.41 respectively). However, donor hypertension had no impact on pancreas allograft survival since day 30 post-transplantation (respectively, HR = 1.22, 95% CI from 0.47 to 3.15), neither on kidney allograft survival (HR = 1.58, 95% CI from 0.80 to 3.10 p = 0.1844). Donor hypertension was uncommon (5.7% of donors) but associated with an increased risk of allograft failure compared to non-hypertensive donors: 12.6% vs 26.9% at one month; 28.8% vs 50.7% at 10 years, p = 0.0037.

**Conclusion:** Despite rare, pancreas transplantation from hypertensive donors is associated with an increased risk of early pancreatic allograft failure, without significant effect on kidney allograft function, suggesting different pathophysiological mechanisms that the ones commonly described as atherosclerosis.

**Table. Results of the multivariable cause-specific Cox model associated with the risk of pancreas graft failure at 30 days post-transplantation (n=786, 113 observations removed because of missing data).**

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BMI, body mass index; CI, confidence interval; HR, hazard ratio. The model was stratified on the center.
Abstracts

343.2

Pancreatic Allograft Thrombosis: Implementation of the CPAT-Grading System in a Retrospective Series of Simultaneous Pancreas-Kidney Transplantation

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Introduction: Pancreatic graft thrombosis (PAT) is a major surgical complication, able to cause graft loss in pancreatic transplantation. The recently proposed Cambridge Pancreas Allograft Thrombosis (CPAT) grading system provides diagnostic, prognostic and therapeutic recommendations.

Methods and Results: We retrospectively studied the incidence and grade of PAT using the CPAT grading system in a series of 344 simultaneous pancreas-kidney (SPK) transplant recipients (grafted from 2005 to 2019), who underwent routine CT imaging. The analysis of CT scans, performed independently by a radiologist and a surgeon, revealed signs of PAT in 215 patients (106 grade 1, 85 grade 2, 24 grade 3). In the present study PAT incidence was high because all the recipients underwent CT scan and all grades of thrombosis were considered, contrasting with the majority of studies, where CT scans were not performed routinely in all the recipients but only in those showing graft dysfunction, or following patient symptomatology, and grade 1 thromboses were not considered. The patients who developed PAT were compared to 104 patients with no signs of PAT at the CT scan.

Demographic data of the two groups (thrombosis and non-thrombosis) did not show any significant difference, except for the higher number of male donors in the thrombosis group. Pancreatic graft survival was significantly shorter in the thrombosis group. PAT was cause of graft loss in 41 recipients (11.9%) during the follow-up, but 37 of them (10.8%) have lost their pancreatic graft within the first 30 post-operative days. Graft loss due to PAT was significantly associated with grade 2 and 3 thrombosis. The risk of graft loss did not differ between recipients with grade 0 or grade 1 thrombosis. In the present study the patients with grade 1 thrombosis had a favorable course since none of them had lost their graft of PAT. On the contrary, patients with grades 2 or 3 were at a significantly higher risk of graft loss due to PAT (7/25 and 17/25, respectively) compared to patients with grades 0 or 1; moreover, whatever the cause of pancreatic graft loss (i.e. pancreatitis or bleeding) the risk was significantly associated with the grades 2 and 3. Other factors influencing the occurrence of graft loss were recipient’s age, the development of hyperglycemia, hemorrhage and abdominal pain. PAT did not influence hospitalization duration or patient survival.

Conclusion: The CPAT grading system was successfully implemented in a large series of SPK transplantations and proved applicable in clinical practice. The indications for anticoagulation remain to be studied, although protocol CT imaging and treatment with anticoagulation for partial thrombosis will be standard approach in our patients.

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Outcomes of Primary Simultaneous Pancreas-Kidney Transplants by Induction Agent in the United States

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Background: Induction immunosuppression choice for simultaneous pancreas-kidney (SPK) transplants varies widely in the United States. We examined the association between induction agents and outcomes of SPK recipients discharged on tacrolimus and mycophenolate.

Methods: We used the Scientific Registry of Transplant Recipients to examine all primary SPK transplants between 2000 and 2020, excluding cross-match positive recipients and those with other induction regimens. We grouped recipients according to induction regimen used into three groups: anti-thymocyte globulin (n=5678), alemtuzumab (n=1199) and IL-2 RA (1593). Delayed graft function, acute kidney and pancreas rejection rates were compared by type of induction. We analyzed the ten-year recipient and composite (kidney and pancreas) grafts survival using Kaplan-Meier survival function. Cox proportion hazard models were utilized to examine the association between induction type and the ten-year recipient and grafts survival. Models were adjusted for recipient age, sex, ethnicity, HLA-MM, diabetes type, dialysis dependency, cold ischemia time, local vs imported organs, PRA, steroid maintenance and PDRI.

Results: Delayed graft function rate was observed in less than 6.5% of the recipients and did not differ between groups P=0.68. One-year kidney rejection rates were observed in 8.9% of the anti-thymocyte group, 9.5% of the IL-2RA group and 13% in the alemtuzumab group (p<0.001). Similarly, one-year pancreas rejection rates were observed in 9.5% of the anti-thymocyte group, 12.4% of the IL-2RA group and 14.1% in the alemtuzumab group (p<0.001). In the univariable analysis, induction type was not associated with recipient (log-rank p=0.11) or grafts survival (log-rank p=0.36). In the multivariable model for the composite grafts survival, alemtuzumab use was associated with 22% increased kidney or pancreas graft loss compared to anti-thymocyte globulin (LLCI, aHR, ULCI) (1.05, 1.22, 1.42), while IL-2RA use was not a predictor of worse grafts survival. Induction type didn’t influence recipient survival in the adjusted model.

Conclusion: r-ATG use was associated with the lowest kidney and pancreas rejection rates. Compared to r-ATG, alemtuzumab but not IL-2RA was associated with worse long-term death-censored SPK grafts outcome. Our analysis supports the US national popularity of r-ATG induction in primary SPK recipients.
Pancreas Transplant Outcomes With No Early Graft Loss at A Single Institution

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Introduction: The reported 3-month graft failure rate for pancreas allograft remains high ranging from 7-22%. We report outcomes and experience from a single institution with no technical graft loss.

Method: A retrospective chart review was conducted of patients who underwent pancreas transplant +/- a kidney transplant from 2012-2021 with a maximum follow-up of five years. Information on pancreas and kidney graft failure was obtained and defined by current 2019 Organ Procurement and Transplantation Network (OPTN) criteria.

Results: There were a total 74 patients included. The average age was 47.2 (+/- 9.97) with an average duration of diabetes of 22 years. 35.1% of patients were White, 40.5% Black and 24.3% other. 25% of patients identified as Hispanic. 70% of patients were male and 30% female. 65% of patients had type I diabetes and 35% type II diabetes. Most patients underwent simultaneous pancreas-kidney (SPK) transplant (92%), 5.4% had pancreas transplant after kidney (PAK) and 2.7% had a pancreas transplant alone (PTA). The 3-month pancreas and kidney allograft survival was 100%. The 1-year survival for both pancreas and kidney were 97%. 5-year survival of pancreas transplant after kidney (PAK) and 2.7% had a pancreas transplant alone (PTA). The 3-month pancreas and kidney allograft survival was 100%. 5% no pancreas graft failure due to vascular thrombosis or technical complications. Reasons for failure include: PTLD. The reported 3-month graft failure rate for pancreas allograft was 90.4% and 91.8% for kidney allograft.

Conclusion: We report improved survival after pancreas transplantation with no early vascular thrombosis or technical complications and good pancreas and kidney allograft survival due to optimization of technique in addition to protocolized pre- and post-operative management protocol.

Four-Year Patient Survival After Simultaneous Pancreas-Kidney Transplantation According to Graft Status Using Kaplan-Meier Survival Method Versus Competing Risk Model

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Background: Cardiovascular events and infections are the leading causes of death after simultaneous pancreas-kidney transplantation (SPKT). Previous studies have shown the graft loss is also related to overall patient survival probability; however, the survival analyses by traditional methods can face bias due to not considering the competing risk between graft losses and death.

Aim: To compare the patient survival submitted to SPKT according to the status of graft losses, kidney, pancreas, or both four years after transplantation.

Methods: This is a retrospective, longitudinal and observational study that enrolled 432 patients submitted to SPKT at Hospital do Rim between 2000 and 2015. The final date follow-up was December 2019. The patients were categorized into four groups according to the graft status: renal graft loss (RL), pancreas graft loss (PL), both grafts losses (BL), and no graft loss (NL).

Results: The frequency of patients and time to graft loss according to groups were: 3.7% for RL, in 14.7 months; 10.6% for PL, in 0.67 months; and 8.6% for BL, in 1.37 months. The 1- and 4-year patients’ survival by Kaplan-Meier were 85.8% and 80.7%, respectively. The age-adjusted risk of death was associated with RL (HR=5.70; P<0.001) and BL (HR=9.60; P<0.001). The higher when analyzed by competing risk: 40.5% vs. 52.4%, and 25.4% vs. 32.6%, one and four years, respectively. Similarly, the Cox regression considering NL as a reference group.

Results: The frequency of patients and time to graft loss according to groups were: 3.7% for RL, in 14.7 months; 10.6% for PL, in 0.67 months; and 8.6% for BL, in 1.37 months. The 1- and 4-year patients’ survival by Kaplan-Meier and competing risk model. The association between graft loss and patients’ survival was estimated by univariable and multivariable models thorough Cox regression, considering NL as a reference group.

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343.6
Outcomes of Simultaneous Kidney-Pancreas Transplantation in Patients With Type-1 and Type-2 Diabetes Mellitus

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1Transplant, John C. McDonald Regional Transplant Center - Willis Knighton Health System, Shreveport, LA, United States.

Introduction: Advantages for type-2 diabetes mellitus (T2DM) patients receiving simultaneous kidney-pancreas transplantation (SKPT) as compared to kidney transplantation are shorter waiting times and availability of better-quality organs. UNOS approved SKPT for T2DM in 2014. We listed patients with T2DM and ESRD for SKPT with the following criteria: (1) age < 55 years, (2) insulin requirement ≤ 1 unit/kg body weight, (3) BMI ≤ 32 kg/m2. The aim of this study was to measure the change in volume of SKPT and compare outcomes between SKPT T1DM and T2DM recipients.

Method: From Feb 2010 to Dec 2021, 62 T1DM and 36 T2DM SKPT recipients were studied. BMI, c-peptide, HbA1c, and e-GFR were evaluated pre-transplant and post-transplant until 1-year. Outcomes included volume of SKPT pre-and post- UNOS approval of SKPT for T2DM, complications, death-censored 5-year kidney and pancreas graft survival, and 5-year patient survival.

Results: Among 98 SKPT, 18 (T1DM) were done before and 80 (44 T1DM and 36 T2DM) after the UNOS approval of SKPT in T2DM, translating to an increase in SKPT from 3.6/year to 11.4/year (216.7% increase) (Figure 1). T2DM patients were older, gained weight post-transplantation, and had higher BMI and e-GFR at 1-year post-transplant (Table 1). There were no differences in complications and graft and patient survival (Figure 2).

Conclusions: UNOS approval of SKPT for T2DM led to an increase in SKPT with no differences in graft or patient survival between T1DM and T2DM patients. Weight gain should be carefully monitored and managed post-transplant in SKPT T2DM recipients.
COVID-19 and Allograft Damage After Simultaneous Pancreas And Kidney Transplantation: Clinical Case Series And Literature Review

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Introduction: The risk for morbidity and mortality from coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is high in transplant recipients due to the continued immunosuppression regimen for allograft maintenance. While SARS-CoV-2 primarily affects the lungs and causes pulmonary sequelae, evidence suggests that infection by the virus affects other organ systems as well. Simultaneous pancreas-kidney (SPK) transplantation is a treatment for patients with insulin-dependent diabetes and end-stage renal failure. Management of COVID-19 is especially challenging in patients who received SPK transplantation due to the complex interaction between the viral pathogenesis, pancreas and kidney allografts, and immunosuppressive therapies. Therefore, examining the clinical management and recovery process of allograft damage in post-SPK transplant patients who contacted COVID-19 could be valuable in establishing optimal treatment guidelines for this vulnerable population.

Methods: We present a series of patients who contacted COVID-19 and developed allograft damage after receiving SPK transplantation at our institution. The following information was retrieved and collated: demographics, baseline health following transplantation, clinical management of COVID-19 infection and allograft damage.

Results: Out of 10 post-SPK transplant patients who tested positive for COVID-19, 5 patients (50%) also developed elevation of amylase and/or lipase levels 3 times the upper limit of normal. The average AlloSure level of these 5 patients was 5.67% at the time of pancreatic damage. One patient contacted COVID-19 after being admitted for acute rejection and inflammation of the pancreas, and recovered after receiving remdesivir, dexamethasone, plasmapheresis, and high dose prednisone with aggressive diuresis. The other patient was diagnosed with pancreatitis and acute kidney injury on admission and had symptomatic improvements after receiving thymoglobulin induction, IVIG, and rituximab. The patient subsequently contacted COVID-19 after discharge and fully recovered after receiving Bamlanivimab infusion, which occurred concurrently with a precipitous decline in amylase and lipase levels. The remaining 3 patients did not meet the criteria for acute pancreatitis, and they recovered after receiving tixagevimab with cilgavimab, remdesivir with dexamethasone, and Bamlanivimab infusion, respectively, along with supportive treatments.

Conclusion: Damage to the allograft via immunological processes and infectious agents is a recurring concern for patients who received SPK transplantation. Notwithstanding the clinical overlap of COVID-19 infection and allograft damage in the reported patients, it is still unclear if COVID-19 infection directly elicits damage. Further research is required to clarify the relationship between these two phenomena and establish an optimal treatment guideline.

<table>
<thead>
<tr>
<th>1-Year Complications, %</th>
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<tbody>
<tr>
<td>Bleeding</td>
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<tr>
<td>Pancreatitis</td>
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<tr>
<td>Thrombosis</td>
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<tr>
<td>Anatomic Leak</td>
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<tr>
<td>Wound Dehiscence</td>
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<tr>
<td>Wound Infection</td>
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<tr>
<td>Abnormal</td>
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<td>Peripancreatic Hematoma</td>
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<tr>
<th>Volume of SKPT before UNOS approval 2010-2014, % (n)</th>
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<tr>
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<tr>
<th>Death censored 5-year kidney graft survival, % (n)</th>
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<td>95.2 (29)</td>
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<th>5-year patient survival, %</th>
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<td>95.2 (29)</td>
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Recipient’s Low-Grade Chronic Inflammation Has an Impact on One-Year Survival After Simultaneous Pancreas And Kidney Transplantation

Michał Maciech1, Tadeusz Grochowiak1, Magdalena Durlik2, Leszek Paczek3, Sławomir Nazarewski3.

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Introduction: Diabetes mellitus type 1 and end-stage renal disease can induce low-grade chronic inflammation (LGCI) which has an impact on simultaneous pancreas and kidney transplantation (SPKTx) recipients. Preoperative LGCI status measured by PLT, ALB and CRP levels have significant impact on one-year survival of SPKTx recipients.

Objectives: To evaluate impact of preoperative LGCI on one-year survival recipients after SPKTx.

Material and methods: Mean observation after SPKTx was 82.7 months (range: 0.1-220). Among 103 SPKTx recipients following parameters of LGCI were assessed directly before transplantation: white blood cells (WBC) [mean: 7.55*103/mm3 (SD±2.56)]; platelets (PLT) [mean: 244.3*103/mm3 (SD±84.03)]; C-reactive Protein (CRP) [mean: 4.5mg/L (SD±4.97)]; albumin (ALB) [mean 4.5(g/dL) (SD±2.13)]; and neumophiles (NEU) [mean: 5.12*103/mm3 (SD±2.13)]. The markers were categorized using Weight of Evidence test (WoE) supported by Information Value test (IV). Uni- and multivariate analysis was performed with ROC curve and area under curve (AUC) was assessed. Cumulative survivals were assessed using Kaplan-Meier curves.

Results: One-year cumulative survival rates was 87.2 % (SD±0.03). During first year deaths due to complications of infections had significantly higher rate than in second to tenth year after SPKTx (89% vs 11%, Fisher test). ALB, CRP, PLT, WBC and NEU were categorized with cut-off points for further analysis: 3.65g/dL, 2.25mg/L, 180*103/mm3, 5.12*103/mm3 and 5.8*103/mm3, respectively. In univariate analysis significant for 12-month survival were: NEU>5.8*103/mm3, PLT<180*103/mm3, CRP>2.25mg/L and ALB<3.65g/dL with odds ratios (OR): 2.97; 6.75; 5.51; 4.05, respectively. In multivariate analysis, there were two models with independent factors for 12-month survival: model 1 (ALB+PLT) with OR: 3.12 and 5.55; and model 2 (CRP+PLT) with OR: 5.51 and 4.3, respectively. AUC for model 1 and 2 were: 0.74 and 0.75, respectively.

Conclusions: Preoperative recipients LGCI status measured by PLT, ALB and CRP levels have significant impact on one-year survival of SPKTx recipients.

Longitudinal Monitoring of Pancreas and Kidney Transplant Recipients Using Donor-Derived Cell-Free DNA

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Introduction: Donor-derived cell-free DNA (dd-cfDNA) is validated for allograft surveillance in kidney transplant recipients; however, the utility in patients undergoing pancreas and kidney (PTx) transplantation has not been well studied. Pancreatic rejection remains a major clinical concern, yet diagnosis relies on pancreatic biopsy which is associated with significant risk of procedural complications. Early identification of allograft injury is imperative to optimize treatment and intervention. Here, we describe dd-cfDNA levels in PTx transplant recipients in the setting of clinical stability and immunological events.

Methods: PTx recipients were monitored longitudinally with dd-cfDNA (AlloSure, CareDx) at the discretion of the treating physician. dd-cfDNA was collected in tandem with standard of care laboratory testing including serum creatinine, amylase, lipase, DSA and BK PCR. Pancreatic graft dysfunction was defined by elevations in serum amylase/lipase or dysregulated glucose control. The reference population was defined by stable allograft function in the absence of immunological or clinical events. Immunological events were defined as clinically suspected allograft rejection or documented subtherapeutic immunosuppression.

Results: A total of 16 PTx patients were monitored longitudinally with dd-cfDNA, including 15 SPK recipients and 1 pancreas after kidney transplant (Table 1). 12 patients met criteria for the stable reference population with a median dd-cfDNA level of 0.22% (IQR 0.12 – 0.36%, n=248). There was a trend towards increased variability in dd-cfDNA levels in the first 2 months post-transplant, after which there was no significant difference in dd-cfDNA stratified by time (Figure 1A). 4 patients developed 6 independent immunological events, which were associated with a significantly increased median dd-cfDNA level of 1.15% (IQR 0.15 – 1.85%) compared to 0.22% in the reference population (p = 0.03, Figure 1B).

Conclusions: In stable PTx recipients, dd-cfDNA levels remain low post-transplant and reflect the reference ranges validated in kidney transplant alone. Early variability in dd-cfDNA levels may be explained by recovery from ischemia reperfusion injury. Significant increases in dd-cfDNA were associated with immunological events including clinically suspected allograft rejection, highlighting its utility in longitudinal graft surveillance.

Table 1: Patient Demographics

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>16</th>
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</thead>
<tbody>
<tr>
<td>Median Age (years)</td>
<td>44.5 (IQR 33.25-49)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9 (56%)</td>
</tr>
<tr>
<td>Female</td>
<td>7 (44%)</td>
</tr>
<tr>
<td>Donor Type</td>
<td></td>
</tr>
<tr>
<td>SPK</td>
<td>15 (94%)</td>
</tr>
<tr>
<td>PAK</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Median Time Post-Transplant (months)</td>
<td>16 (IQR 13.75-25)</td>
</tr>
</tbody>
</table>

Figure 1: A) dd-cfDNA levels in stable PTx recipients stratified by time post-transplant [months]. B) dd-cfDNA levels in stable PTx patients compared to those with immunological events. Boxes represent median and IQR, whiskers represent 10th – 90th percentile.
343.10

A Novel Approach for Pancreas Transplant With Arterial Patch

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1Shiraz Transplant Center, Abu-Ali Sina Hospital, Shiraz University of Medical Sciences, Shiraz, Iran (Islamic Republic of); 2Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran (Islamic Republic of); 3Transplant Research Center, Shiraz University of Medical Sciences, Shiraz, Iran (Islamic Republic of).

Introduction: Since 1966, when Kelly and Lillehei performed the first pancreas transplant (PT), the technique was changed several times. Owing to improvements in immunosuppression and achievements in surgical methods, better outcomes have been reached, and PT has been set as the treatment of choice for patients with concurrent diabetes mellitus and end-stage renal disease.

Methods: In Shiraz Transplant Center, many techniques and approaches for PT are recruited based on the graft and recipient’s condition; recently, a new approach has been examined. In this technique, the common hepatic artery is assigned to the liver during organ procurement (Figure 1). The celiac trunk and superior mesenteric artery are anastomosed to the common iliac artery on the common patch (Figure 2).

Results: Between 2021 April to 2022 February, fifty-nine PT was performed in which thirty-nine of them were with this approach. This led to a dramatic increase comparing to the numbers in the year before (30). The primary outcomes of this technique, including pancreatitis, rejection, and death, are significantly promoted and summarized in Table 1.

Conclusion: Via this method, thanks to reduced cold ischemic time and the number of anastomoses, due to the lack of need for Y graft, the outcomes and also numbers boosted remarkably. However, this technique should be implemented and examined in other centers.
New Arterial Reconstruction Technique Among Simultaneous Pancreas-Kidney (SPK) Transplantation: A Randomized Clinical Trial

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Introduction: Pancreas transplant is the most physiologic therapy for the diabetic patient. Pancreas transplantation is most commonly performed in conjunction with a kidney transplant, a procedure referred to as simultaneous pancreas-kidney (SPK) transplantation. Despite over two decades of experience and the considerable refinements in the surgical techniques, the operation still carries a high morbidity. It theorized that surgical complications following SPK result from the devascularization of the pancreas allograft during the combined liver-pancreas procurement. In this study we are approaching a new arterial reconstruction technique amongst SPK aiming to reduce pancreatic manipulation hence postoperative complications.

Methods: This Trial was performed in from October 2020 to December 2021 in Shiraz Transplant Center, Shiraz, Iran. Inclusion criteria was all patients over 18 years of age undergone SPK tx due to diabetic nephropathy. For venous anastomosis, the superior mesenteric vein (SMV) is clamped at the mesenteric root. After venotomy of SMV, an end-to-side anastomosis is performed from the portal vein to SMV with standard vascular anastomosis technique. then the patients randomized for Arterial reconstruction: arterial reconstruction is performed with a Y graft anastomosis to the right common iliac artery (CIA) or, a Y graft with two short arms is selected in a bench surgery, and an extension graft from the carotid is prepared for anastomosis to the CIA. The primary outcomes were evaluation of postoperative complications such as pancreatitis, vascular events, fistula formation, intra-abdominal bleeding, and rejection in the first six months after SPK transplantation in these two different arterial reconstruction technique.

Results: A total of 30 patients were included in this study, of which 15 were in each group. The mean age of patients was 33.3 ± 6.3 years. 19 patients were male and 11 patients were female. Table 1 shows demographic data between the two groups.

According to results of table 2, rate of pancreatitis, vascular events and rejection was less in the Y- graft and extension technique, although this difference was not statistically significant. No mortality was observed during the study period. Cohen’s coefficient for Y graft and extension technique regarding pancreatitis, venous thrombosis, rejection was 0.5, 0.57 and 0.61, respectively which means a medium-sized effect.

Conclusion: The results of our study showed that the Y- graft and extension technique reduces postoperative complications such as pancreatitis, vascular events and rejection without increasing the length of surgery time.
Pancreas Transplants Alone - Why Are Not More Done?

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Introduction: In contrast to non-pancreatic transplantation, where nephrologists refer patients for kidney and hepatologists for liver transplantation, endocrinologists only rarely refer patients with brittle diabetes for solitary pancreas transplantation. While most pancreas transplants are performed in combination with a kidney graft, solitary pancreas transplants (PTA) without a previous kidney transplant accounted for only 6-7% of pancreas transplants per year although a PTA is the best treatment option to achieve long-term insulin-independence in patients with severe brittle diabetes.

Methods: The change in demographics and outcome of 1,636 primary PTAs from deceased donors were analyzed between 1/1/2001 and 12/31/2020 in 5-year intervals. Graft survival was defined as complete insulin-independence. Multivariate analysis was performed to assess factors that impacted on short- and long-term outcome and the potential need for a subsequent kidney transplant.

Results: Over time, recipient age increased, but donor age and preservation time decreased significantly. Most recipients received induction therapy and maintenance immunosuppression with tacrolimus and MMF. These changes resulted in significant improvement in patient and pancreas graft survival. Three-year patient survival increased from 92% in 2001-05 to 96% in 2016-20. Three-year pancreas graft survival improved from 60% in 2001-05 to 77% in 2016-20 (p<0.0001). While the early technical failure rate did not significantly change over time and remained stable around 6-7%, the immunological graft loss rate in technically successful transplants dropped significantly at 3-years from 24% in 2001-05 to 13% in 2006-20 (p<0.01). By multivariate analysis, the most influential factors for this decrease were older recipient age and better immunosuppression. Donor factors (age, preservation time, HLA matching) did not show any impact, possibly due to an excellent donor selection process. Transplants at high volume transplant centers showed a significantly better outcome.

Due to better donor and recipient selection, refinements in immunosuppression, and improvements in graft outcome the rate of a subsequent kidney transplant declined significantly. This rate was primarily contingent on native graft function at the time of the pancreas transplant. If the GFR was <50ml/min, 27% of patients received a kidney graft 5-years after the pancreas transplant; if the GFR was >70ml/min only 1% of patients required a kidney graft.

Conclusion: Our study shows that the results of PTA have significantly improved over the past 20 years. A PTA should be strongly considered in brittle diabetic patients before the development of advanced nephropathy. Although the risk of immunological failure has also significantly decreased, results are best in recipients > 30 years of age.

C-Reactive Protein and Urea Levels Distinguish Primary Non-function From Early Allograft Dysfunction After Liver Transplantation

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Introduction: A spectrum of graft dysfunction occurs after liver transplantation (LT), ranging from early allograft dysfunction (EAD) to primary non-function (PNF). There are no single or uniformly accepted laboratory parameters that differentiate these entities. Several biochemical markers are exclusively made in the liver, including urea, C-reactive protein (CRP) and fibrinogen. However, these are given less prominence than transaminases, bilirubin and International Normalised Ratio (INR). The aim of this study was to determine if routinely measured serum biochemical markers can distinguish PNF from EAD in the initial 48 hours following deceased donor liver transplantation.

Methods: A retrospective study of all adult patients that underwent LT at our institution between January 2010 and April 2020 was performed. Patients that experienced graft loss from a complication other than PNF in the initial 14 days were excluded. Patients were grouped into an immediate graft function (IGF), EAD, and a PNF groups. The absolute values and trends of CRP, blood urea, serum transaminases, INR and fibrinogen in the initial post-operative 48 hours were compared between groups. Biochemical factors found to be significantly different between groups on univariable analysis were further investigated using receiver operating characteristic (ROC) curves. The area under the receiver operating characteristic curve (AUROC) value was reported, and the Youden index was used to identify the optimum cut-off values.

Results: During the study period, 2102 LTs were performed and 1937 were eligible for inclusion. There were 1394 patients with IGF (72%), 503 with EAD (26%) and 40 with PNF (2%) patients according to the study definition. A significantly greater proportion of grafts were from donors following cardiac death (DCD) in the PNF group compared to the EAD group (45% vs. 29%; p=0.04). The median (IQR) of each variable and the accuracy in distinguishing PNF from EAD is demonstrated in table 1 and 2 respectively. Lack of an increment in CRP (Day 1: 1.43 v 1.77, P=0.01) and urea production between on day 1 and 2 (Day 1: 0.71 vs 1.32, P=0.01) were significant. The CRP level was significantly lower on post-operative day 2 in the PNF group (Day 2: 1.32 vs 1.77, P=0.01). The median (IQR) of each variable and the accuracy in distinguishing PNF from EAD was calculated using receiver operating characteristic (ROC) curves. The area under the receiver operating characteristic curve (AUROC) value was reported, and the Youden index was used to identify the optimum cut-off values.

Discussion: CRP and AST are more effective than ALT and bilirubin in distinguishing PNF from EAD in the initial post operative 48 hours. Clinicians should consider the values of these markers when making treatment decisions for patients with early liver allograft dysfunction.
Delta Changes in Donor-Derived Cell-Free DNA (dd-cfDNA) Complement the Donor Fraction in Kidney Transplant Surveillance

Alexander Wiseman1, Gaurav Gupta2, Muralidharan Jagadeesan2, Vinaya Rao3, Mohanram Narayanan3, Nikhil Agrawal4, Grigory Shekhtman4, Yi Fu5, Kevin Pinney5, Sanjiv Anand5

1Medicine, Centura Health-Porter Adventist Hospital, Aurora, CO, United States; 2Medicine, Virginia Commonwealth University, Richmond, VA, United States; 3Medicine, George Washington School of Medicine, Washington DC, DC, United States; 4Medicine, Intermountain Healthcare, Murray, UT, United States; 5Medicine, Baylor Scott and White, Austin, TX, United States; 6Kidney Transplant, CareDx, Brisbane, CA, United States; 7Medicine, Medical University of South Carolina, Charleston, SC, United States.; KOAR registry.

Introduction: Delta changes in dd-cfDNA levels over time may identify patients with evolving allograft injury, providing complementary information to the donor fraction. We explored the dd-cfDNA trajectories preceding biopsy-proven rejection (BPAR) events among kidney transplant recipients enrolled in theKidney allograft Outcomes AlloSure Registry (KOAR, NCT03326076) and undergoing longitudinal surveillance with dd-cfDNA.

Methods: In the primary analysis, we compared the change in dd-cfDNA from baseline to the time of BPAR (for-cause or surveillance biopsies). We identified patients with first-time rejection events and at least 3 prior dd-cfDNA results; the index result was obtained ≤30 days before BPAR; we then selected the lowest of two preceding results as the patient-specific baseline and compared this with the index result. We then analyzed patients with rejection (first or subsequent, at least 90 days apart) and ≥2 dd-cfDNA results, including one within 30 days of the index biopsy. The reference change value (RCV) was calculated using an allograft reference population of patients with stable allograft function, at least 3 dd-cfDNA measurements, and no significant clinical events.

Results: A total of 28 patients with BPAR met criteria for the primary analysis; among these, median baseline dd-cfDNA was 0.22% (IQR: 0.19 - 0.35) and median dd-cfDNA at the time of rejection was 1.35% (IQR: 0.75 - 2.75), representing a 491% (IQR: 177 - 1133) increase between these results, obtained 71.5 (IQR: 46 -113) days apart (Table 1A). 51 events met criteria for the second analysis where a median increase of 253% (IQR: 72 - 821%) between sequential dd-cfDNA values obtained 69 days (IQR: 45 - 108) apart preceded biopsy-proven rejection events (Table 1B). The calculated RCV for the stable reference population within KOAR was 56.3%. 39 of these 51 events (76%) demonstrated increases greater than this RCV.

Conclusions: Longitudinal surveillance with dd-cfDNA allows the integration of delta changes and trajectories over time, allowing earlier identification of evolving allograft injury. Significant changes from an established baseline and between sequential values ahead of biopsy-proven rejection highlight how longitudinal surveillance may improve diagnostic performance.

Delta Changes in Donor-Derived Cell-Free DNA (dd-cfDNA) Complement the Donor Fraction in Kidney Transplant Surveillance

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Introduction: Delta changes in dd-cfDNA levels over time may identify patients with evolving allograft injury, providing complementary information to the donor fraction. We explored the dd-cfDNA trajectories preceding biopsy-proven rejection (BPAR) events among kidney transplant recipients enrolled in the Kidney allograft Outcomes AlloSure Registry (KOAR, NCT03326076) and undergoing longitudinal surveillance with dd-cfDNA.

Methods: In the primary analysis, we compared the change in dd-cfDNA from baseline to the time of BPAR (for-cause or surveillance biopsies). We identified patients with first-time rejection events and at least 3 prior dd-cfDNA results; the index result was obtained ≤30 days before BPAR; we then selected the lowest of two preceding results as the patient-specific baseline and compared this with the index result. We then analyzed patients with rejection (first or subsequent, at least 90 days apart) and ≥2 dd-cfDNA results, including one within 30 days of the index biopsy. The reference change value (RCV) was calculated using allograft reference population of patients with stable allograft function, at least 3 dd-cfDNA measurements, and no significant clinical events.

Results: A total of 28 patients with BPAR met criteria for the primary analysis; among these, median baseline dd-cfDNA was 0.22% (IQR: 0.19 - 0.35) and median dd-cfDNA at the time of rejection was 1.35% (IQR: 0.75 - 2.75), representing a 491% (IQR: 177 - 1133) increase between these results, obtained 71.5 (IQR: 46 -113) days apart (Table 1A). 51 events met criteria for the second analysis where a median increase of 253% (IQR: 72 - 821%) between sequential dd-cfDNA values obtained 69 days (IQR: 45 - 108) apart preceded biopsy-proven rejection events (Table 1B). The calculated RCV for the stable reference population within KOAR was 56.3%. 39 of these 51 events (76%) demonstrated increases greater than this RCV.

Conclusions: Longitudinal surveillance with dd-cfDNA allows the integration of delta changes and trajectories over time, allowing earlier identification of evolving allograft injury. Significant changes from an established baseline and between sequential values ahead of biopsy-proven rejection highlight how longitudinal surveillance may improve diagnostic performance.
Extracellular Vesicles Released During Normothermic Machine Perfusion Are Associated With Human Donor Kidney Characteristics

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Background: Extracellular Vesicles (EVs) represent stable, tissue specific nano-sized particles that reflect the conditional state of their tissue of origin. Here, the dynamic release and phenotype of kidney EVs was characterized and quantified during Normothermic Machine Perfusion (NMP) of Expanded-Criteria Donor (ECD) kidneys to examine whether EVs could function as a potential biomarker for assessing kidney quality before transplantation.

Materials & Methods: Eight discarded ECD kidneys (~13 ± 5 hours of cold ischemia, age 68 ± 7 (mean ± standard deviation), all male) were perfused in a closed system at 37 °C for 6 hours. Perfusates were taken before and at 1, 3 and 6 hours of NMP and examined with Nanoparticle Tracking Analysis (NTA) and Imaging Flow Cytometry (IFCM). For IFCM, perfusates were stained with the tetraspanins CD9, CD63 or CD81 (general EV markers), or a mix of these three markers in combination with CFDA-SE (a non-fluorescent molecule that acquires fluorescent properties after cleavage by intravesicular esterases) to identify, quantify and characterize EVs.

Results: Analysis of perfusates with NTA revealed that the majority of nano-particles present in the perfusates are <300 nm. For CFSE and the mix of tetraspanin double-positive EVs, we observed a ~700/ 740/ 560 fold increase compared to EV levels before perfusion at 1, 3 and 6 hours of NMP, respectively. Analysis of EV concentrations with crude donor characteristics (e.g. age, cold ischemia time (CIT), kidney weight) and NMP viability characteristics (renal flow, renal flow resistance, urine production) revealed that double-positive EV are negatively correlated with CIT whilst positive correlations were found with donor age after the first hour of NMP. Furthermore, tetraspanin CD81 was found to represent the majority (~75%) of the excreted double-positive EV (CD9: ~16%/ CD63 ~8%) (Figure).

Conclusion: EVs <300nm are released by ECD kidneys during NMP with highest excretion levels during the first hour of perfusion. Tetraspanin CD81 is predominantly present on these EVs, and EV concentrations were shown to be correlated with well-established indicators of kidney quality such as donor age and CIT. The characterization of the excreted EVs as well as their correlation with clinical parameters provide a starting point to study their role as potential biomarkers of kidney quality.

344.3

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Kidney Release of Inflammatory Mediators Is Modulated by 17BETA-Estradiol Associated With Methylprednisolone After Brain Death in Female Rats

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Introduction: Brain dead donors are an important source of organs for transplantation. Brain death (BD) triggers systemic alterations and these patients present higher inflammatory profile in comparison to other types of donors. Also, organs from females patients present worse prognostic in comparison to male organs. This scenario is associated with increased inflammation due to acute reduction of females sex hormones after BD, especially estradiol (E2). In females, evidences suggest that the presence of both E2 and corticoids hormones is important to ensure an adequate response to inflammation. The aim of this study is to evaluate the associated treatment of E2 and methylprednisolone (MP) in female rats after BD.

Methods: Female Wistar rats were submitted to BD by rapid inflation of an intracranial balloon catheter and maintained for 6h. Rats received MP (MP , 4 mg/ml i.v–2 ml/h) or MP and E2 (MP/E2, 50 ug/ml) after 3h of BD until the end of experiment. Sham-operated (S) rats were used as controls. After 6h, kidney samples were collected for tissue homogenate and relative gene expression analyzes. IL-1β, IL-6, IL-10, VEGF and TNF-α were quantified in tissue homogenate. Gene expression of IL-1β, IL-6, IL-10, TNF-α and KIM-1 was also evaluated.

Results: In kidney tissue homogenate, IL-6 (p=0.0076) and VEGF (p=0.0241) were increased after BD, and both molecules were reduced after the treatment. Regarding IL-10 (p=0.0624) and TNF-α (p=0.0255), there was no difference between S and BD groups, but there is a significant reduction in both treatments. There were no differences in IL-1β. Regarding relative gene expression, there were no differences among groups in any of the molecules analyzed.

Conclusion: Our data pointed that, after BD, females rats presented higher inflammation in the kidney in comparison to Sham animals, represented by an increase in tissue release of cytokines, especially IL-6. Results suggest that both treatments are able to reduce kidney acute inflammation. These data propose that corticotherapy and its association with E2 has a potential benefic effect in inflammation triggered by BD in kidneys from females donor, suggesting that this treatment may improve organ quality.

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Reduced Epidermal Growth Factor (EGF) Expression During Antibody Mediated Rejection Following Heart Transplantation

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Antibody mediated rejection (AMR) remains one of the major challenges for long-term survival following heart transplantation. The immediate and long-term impact of HLA antibodies on graft survival is well established. However, the signaling pathways that are involved in AMR are not well established. Endothelial cell activation by HLA antibodies lead to the activation of several downstream signaling pathways. We utilized an in vitro human endothelial cell model treated with humanized monoclonal antibodies to HLA Class I antigens to identify the signaling pathways involved in AMR. A reduction of epidermal growth factor (EGF) levels in endothelial cells was observed following coupling these cells with HLA antibodies. We confirmed this result with ELISA assays of the cell culture supernatant of endothelial cells treated with humanized monoclonal antibodies to HLA class I antigens (mean 32 pg/ml ±SD 4.5 vs control cells 53 ±SD 7.2 pg/ml). Serum EGF levels were evaluated in heart transplant recipients with and without AMR. In patients with AMR (n=16), the mean serum EGF levels were significantly reduced as compared to patients with no AMR (n=22) (151.6± SD 73 pg/ml vs 237.4± SD 52.94 pg/ml, p <0.05). Our data indicates reduced EGF expression in heart transplantation recipients with AMR. This reduction might suggest that EGF could have a protective effect in heart transplant recipients during AMR. This is the first study to demonstrate a correlation between serum EGF levels and AMR in heart transplant recipients.
QSant, a Urine-Based Multi-Analyte Assay, Detects And Predicts Acute Rejection Risk With High Accuracy, in the First 2 Weeks Post-transplant

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Introduction: Current blood-based biomarker assays are confounded by ischemic reperfusion injury(IRI) and have an inability to detect acute rejection(AR) in the early post-transplant(9) period. Some of these assays fail in the first two weeks, and others fail even in the first 90 days post-transplant. We proposed to evaluate if the urine biomarkers-based assay – QSant [Yang, STM 2020], could accurately detect biopsy confirmed AR in functioning allografts in the first 2 weeks post-transplant.

Methods: 27(sensitized=4, cPRA >20%) adult renal allograft recipients (69% deceased donors), on basiliximab induction and TAC/MMF/CS maintenance, with (n=18) and without (n=9) biopsy confirmed AR (NPAR), had serial urine samples (n=96) bio-banked in the first 2 weeks, at cause biopsy and at 6 months. First episode of AR occurred at 8 days(median) post-tx and 69% of the early AR were refractory requiring Alemtuzumab. QSant was run on all urine samples, and the following clinical risk categories identified: i) immune- quiescence (IQ): Q-Score <32 and ii) acute rejection (AR): Q-Score >32. The latter range was further sub-divided into a dynamic alloimmune injury spectrum: 32≥QScore≤55; and a high-grade acute rejection: Q-Score >55 [Sarval, JCM 2022]. Analyses comprised of:i) Cross-sectional correlation between the Q-Score, SCR and BPAR; (ii)Longitudinal immunosuppression (IS) treatment response-correlation with QSant.

Results: BPAR occurred in 66% of patients; 11/18 cases occurring in the first week post-tx. The accuracy of QSant to detect early BPAR(< 2 weeks post-tx) was 89.3% this is in contrast to the median change in SCR by +15%. QSant detected both ABMR and TCMR. The median Q-Scores for 5 cases of ABMR were lower at 30(QR:25-43) compared to 13 cases of TCMR at 49(QR:29-85). In 44% of cases elevated Q-Scores >32 was observed preceding BPAR by 3 days(median), supporting the ability of QSant to predict the risk of AR across the alloimmune injury spectrum. Refractory BPAR cases (n=9) had higher Q-Scores than treatment sensitive rejections (Q-Score: 50(QR:31-86) versus 32(QR:19-41)). This differential was statistically signifi- cant (p=0.008) attesting to treatment sensitive rejections encompassing the alloimmune injury spectrum and refractory events being more of high-grade AR. Repeat QSant monitoring post treatment of refractory BPAR registered a 25% decline(median) in response to IS treatment.

Conclusions: QSant trajectory tracking by serial urine analysis early post-transplant, can potentially obviate or trigger for-cause biopsies. Despite the sampling size, urinary QSant-based AR diagnosis is not confounded by early ischemia reperfusion injury and very early time post- transplant. This under- scores the potential to augment clinician decision-making during the early weeks post-transplant, to diagnose AR.

Early Post-operative Thrombotic Microangiopathy in Deceased Donor Kidney Transplant: Case Series

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Background: Thrombosis associated thrombotic microangiopathy (TA-TMA) is well recognized as a serious complication of renal transplantation. TA-TMA is characterized by injury of arterioles and capillaries and encompasses syndromes of thrombocytopenia, microangiopathic hemolytic anemia(MAHA) and variable degrees of kidney graft dysfunction. TA-TMA can be classified into recurrent TMA (from underlying complement mutations) and de novo TMA. The incidence of de novo TMA ranges from 3-14%. Causes of de novo TMA include immunosuppressive drugs (tacrolimus, mTOR inhibitors, basiliximab), ischemia reperfusion injury(IRI) and have an inability to detect acute re-jection(AR). Repeat QSant monitoring post treatment of refractory BPAR registered a 25% decline(median) in response to IS treatment.

Conclusions: Despite the many of these cases also have very low levels of ADAMTS13 but do not meet clinical criteria for TTP. If the latter is secondary to endothelial dam- age vs consumption process is still unknown.

Objective: The purpose of this study was to identify if any specific risk fac- tors or variables are associated with TA-TMA in the setting of deceased donor kidney transplantation (Dx) in the immediate post-operative period (defined as less than 2 weeks from transplant date) since January, 2017. We analyzed donor characteristics including age, type of deceased donor, last known platelet count, biopsy features, pump parameters, cold ischemia time (CIT), warm ischemia time (WIT), reperfusion injury (RI) described at transplant surgery. The context we assembled included baseline platelet count on admission, the post-op day of diagnosis and at resolution (defined as platelet count > 100K and no need for additional transfusion), the use of thymoglobulin, ADAMS13 activity, changes in maintenance immunosuppression, evidence of post op bleeding, delayed graft function (DGF) and its recovery, and renal function at 1 and 3 months post transplant (Table).

Results: 72% of the kidneys were from donation after cardiac death (DOCD). The mean arterial pressure on the perfusion pump was 39 ± 7 mmHg and the flow was 148 ± 55 ml/sec. 81 % of the donor biopsies showed mild ATN, 72% had evidence of atherosclerosis and 54% of fibrosis and only one showed fibrin thrombi in the glomerulus. The mean CIT and WIT were 1913 ± 423 and 27 ± 32 min, respectively. The mean donor platelet count and LDH level 2880 ± 55 U/L. 3 patients received FFP infusions, 5 received plasmapheresis and 3 received conservative treatment. The micro- angiopathic hemolytic anemia recovered in 10 ± 2.4 days to a platelet count of 130 ± 67 x 10(3)/mcl. There were 6 cases of post op bleeding (55%) with 4 requiring surgical intervention and 4 cases of RI (36%). Of the 8 patients that sustained DGF, 6 recovered after one month, one recovered after 3 months post transplant (having history of low C3 and late biopsy proven TMA) and one died. The mean SCR and eGFR in TMA and non-TMA were 51 ± 34 and 1 ± 0.5 mg/dl and 66± 30 ml/min, respectively. There were no statistical differences on the above parameters when the patients were grouped by the presence of post operatory bleeding. However, when we added the reperfu- sion injury factor, we found a lower ADAMS 13 levels of 17 ± 7 UI/dl in the non bleeding group who sustained RI (60%) vs 21 ± 37 UI/dl in the bleeding group who had only one patient with RI (17%) (p=0.24).

Conclusions: TA-TMA in the immediate postoperative period can be difficult to diagnose and treat. Our findings demonstrated that 55% of the cases were associated with post operatory bleeding leading to the reduction of ADAMS 13 levels, most likely by platelet consumption. 36% were related to reperfusion injury where the consumption of ADAMS 13 could be explained by direct endothelial damage. None of the patients needed other than con-servative therapy. This data needs to be correlated in a larger cohort. In this context we are planning to prospectively study ADAMS 13 activity in the immediate post kidney transplant period.
The Plasma Level of Transforming Growth Factor Beta 1 in Heart Transplant Recipients: Relationship With HLA Mismatch

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Introduction: Transforming growth factor beta 1 (TGF-beta1) is a pleiotropic cytokine produced by almost all cells of the body and has multidirectional autocrine and paracrine effects. Current research indicates a possible role for TGF beta1 in the development of cardiac allograft rejection and fibrosis after heart transplantation.

The aim: to evaluate the level and dynamics of TGF-beta1 in patients with chronic heart failure and in cardiac recipients and its relationship with HLA mismatch.

Methods: 161 patients were examined before and after heart transplantation, aged 49±12 (from 16 to 78) years, 141 (87%) of them were men. Initial diagnosis was dilated cardiomyopathy in 89 (55%) patients. The comparison group consisted of healthy adults (n=12) - liver donors aged 30 ± 6 years, including 5 men (42%). All patients underwent heart transplantation from an identical or AB0 matched donor. Before transplantation, all patients had their blood group determined, and HLA typing of the A, B, DR loci was performed using the polymerase chain reaction. The concentration of TGF beta1 was determined in blood plasma samples before, one month and one year after transplantation by ELISA.

Results: The average plasma level of TGFbeta1 in the patients with terminal heart failure was 27.2± 18.8 ng/ml and was significantly higher than in healthy individuals 8.7 ± 7.5 ng/ml (p= 0.00). The level of TGF-beta1 did not differ in men and women (p=0.7), and did not depend on the initial diagnosis (p=0.27) and blood type (p=0.8). Heart transplantations identical in blood type were performed in 86% of cases, compatible - in 14%. The proportion of mismatch (MM) according to the HLA system was: MM6=14%, MM5=35%, MM4=32%, MM3=14%, MM2=5%. One month after heart transplantation, the plasma level of TGF-beta1 decreased to 11.1 ± 7.7 ng/ml (p = 0.00) and did not differ from the amount of MM. A year after transplantation, the plasma level of TGFbeta1 was 10.2 ± 10.5 ng/ml and significantly differed from the level before transplantation (p=0.00). In patients with MM4, the level of TGF beta1 was significantly higher than with MM6 (12.7±11.0 ng/ml vs 5.5±4.5 ng/ml, p=0.048). It was found correlation between plasma level of TGF-beta1 and blood concentration of tacrolimus a year after HTx (r=0.148, p=0.04). However, the plasma level of TGF-beta1 didn’t differ in recipients with and without myocardial fibrosis (p=0.42).

Conclusion: In patients with chronic heart failure the plasma concentration of TGF-beta1 is higher than in healthy individuals, and significantly decreases in recipients after heart transplantation. A relationship was found between the level of TGFbeta1 and the amount of MM, which requires further research.
Clinical Grade CD8+T Regulatory Cells Moving Forward in Human Transplantation

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Introduction: We have demonstrated the therapeutic potential of human polyclonal and antigen-specific CAR-modified CD8+ Tregs cell therapy to prevent alloimmune human skin transplantation rejection and xenogeneic GVHD in humanized NSG mice (Bélizia et al., Front Immunol. 2017, Blood Adv. 2019). However, their potential has never been evaluated in a clinical trial. We are thus preparing the launch of a phase I/IIa human clinical trial using polyclonal CD8+ Tregs cell therapy in living donors kidney transplant patients.

Method: CD8+ cells were isolated from blood of healthy volunteers and patients with kidney failure by Clinimacs System then CD8+CD4-CD45RClow/-CD56- T cells were sorted by MACSQuant Tyto cell sorter. Cells were stimulated with anti-CD3 and CD28 mAbs every week and cultured in presence of rapamycin, IL-2 and IL-15. Cytotoxicity against allogeneic PBMCs was assessed by Annexin V/DAPI staining and suppression capacity was assessed in vitro on syngeneic CD4+T cells proliferation in response to allogeneic APCs and in vivo on 1.5 Gy-irradiated NSG mice co-injected with human PBMCs.

Results: We developed a new GMP-compatible cell manufacturing process. First, we determined a new method of isolation of CD8+ Tregs from peripheral blood using a safe closed system. Next, we identified the optimally compatible culture medium, refined cytokines doses and stimulation methods to preserve a high proliferation rate, phenotypic profile and suppressive function of CD8+ Tregs. Using this process, we were able to efficiently expand CD8+ Tregs from peripheral blood of patients with renal failure, with high purity, while preserving their regulatory function. We confirmed the absence of cytotoxicity. In addition, we showed that CD8+ Tregs were phenotypically and functionally stable for 4h after conditioning, which is important for the logistic delay between cell harvest and patient infusion. Finally, we showed that CD8+ Tregs persist for more than 90 days in NSG mice without inducing any signs of xenogeneic GVHD, and could withstand combined immunosuppressive drug therapy administered to the patient.

Conclusion: We designed a clinically compatible manufacturing process to isolate and culture CD8+ Tregs from renal failure patients that preserves their function and patient safety.

Unravelling the Molecular Footprint of Kidney Graft Quality: From Subjective Assessment to Tailored Treatment

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Individual kidney grafts are exposed to damage in different ways (e.g., donor type, donor age) and it is likely that the underlying molecular mechanisms differ. In addition, 20% of donor kidneys are judged irreparably damaged and discarded, primarily due to lack of knowledge regarding the underlying pathophysiological mechanisms. Knowledge of protein degradation leading to loss of tissue integrity and function is particularly scarce. We therefore sought to gain molecular insights into the role of protein (degradation) dependent mechanisms associated with different donor characteristics of kidney grafts. Renal cortex biopsies were collected from deceased donor kidneys (n=15), which were declined for transplantation due to medical and logistical reasons. Biopsies, collected after cold preservation, were analyzed using a combined proteomics and degradomics approach in a non-biased manner. Kidney grafts were classified based on donor characteristics (Table 1). PANTHER pathway enrichment and STRING functional analysis were used to link proteins to biological processes. TopFind analysis was used to match degradation products to their associated protease.

Kidneys from brain dead donors showed enrichment of respiration and energy related processes, and degradation occurred mostly in plasma related proteins residing in tissue material (Figure 1). Kidneys from donors after circulatory death revealed degradation of structural proteins. Older donors exhibited protein enrichment of processes related to immune response and complement activation, but degradation of apoptotic related proteins and proteins responsible for cytoskeletal cleavage. Conversely, younger donors revealed enrichment of mitochondrial and aerobic electron transport related processes, while degradation mostly occurred in proteins related to cell binding. Donors with a BMI of <25 also exhibited enrichment of respiration and energy related processes, but degradation of antioxidants and proteins related to cytoskeletal organization. Donors with an BMI of >30 showed shifted degradation of proteins related to fatty acid metabolism, degradation processes and ATP synthesis. Male donors revealed enrichment of processes related to immune response and complement activation, however showed degradation of mitochondrial proteins. Female donors showed degradation of proteins related to the proteasome complex, and structural proteins. Pathway enrichment analysis revealed different biological pathways upregulated depending on donor characteristics, confirming unique molecular footprints of kidney grafts. Furthermore, proteome and degradome pathways were not always aligned, indicating a potential complex interplay between protein dysregulation and proteolysis. These results reveal novel insights into the pathophysiological mechanisms of deceased donor kidney quality and could lead to novel drug targets for tailored treatment of donor kidney grafts.

Proteomics experiments were funded by Novo Nordisk, awarded to Benedikt Kessler. Machine perfusion experiments were funded by Dutch Kidney Foundation awarded to Ian Alwayn as part of the clinial PROPER trial (NCT04693325). Travel to Oxford was supported by Stichting de Drie Lichten and the Graduate School of Medical Sciences of the University of Groningen, awarded to Leonie van Leeuwen.

Table 1: Donor characteristics of kidney grafts (n=15).

<table>
<thead>
<tr>
<th>Donor characteristics</th>
<th>Mean±SEM</th>
<th>10±2</th>
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</thead>
<tbody>
<tr>
<td>Cold ischemia time (hours)</td>
<td>85±2,4</td>
<td>109,2</td>
</tr>
<tr>
<td>Donor type</td>
<td>DBD</td>
<td>56%</td>
</tr>
<tr>
<td>Donor age (years)</td>
<td>60±6</td>
<td>66</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>&gt;25</td>
<td>25%</td>
</tr>
<tr>
<td>Donor sex</td>
<td>M</td>
<td>89%</td>
</tr>
</tbody>
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DBD: donation after brain death, DCD: donation after circulatory death, BMI: body mass index
### Master Education: A New Era of Teaching Beyond COVID-19

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**Introduction:** University of Barcelona together with Donation and Transplantation Institute offer since 2004 a Master degree in Donation and Transplantation. Since 2011, the program had a blended modular structure including: Donation, Transplantation, Management, Tissue Banking & Advanced Therapies, and Internship (IS). In 2020, due to COVID-19 restrictions, the program was pushed to be adapted to be fully online using innovative resources. The aim is to analyze the impact of the new tools and online teaching modality on the grades and the student’s satisfaction.

**Method:** The syllabus has remained stable since 2020 although the educational modality has been renewed. Until 2019, face to face training included classical theoretical sessions, simulations, clinical cases debate and group exercises. IS were face to face in associated centres located in European and American countries. Since 2020, theoretical sessions have been digitized and introduced into the virtual classroom and practical simulations have been replaced by live sessions (broadcast sets, video analysis, case debates and group exercises). New online tools, as immersive training, have been employed to substitute IS. For IS, a virtual reality tour to a simulated tertiary Spanish hospital including the different units related to donation and transplantation allows interaction with the staff and evaluation of participants through the resolution of cases that arise during the visit. Data are organized in 2 periods for each module including IS, 2011-2019 and 2020-21, and the grades obtained in each module and the students’ satisfaction are evaluated.

**Results:** In 2011-2019, the average grades were: Donation 7.7/10, Transplantation 8.2/10, Management 8.1/10, Tissue Banking & Advanced Therapies 7.6/10 and IS 9/10. And in 2020-2021 the score was 8.6/10, 7.8/10, 8.44/10, 7.9/10, 9.1/10 respectively. In 2011-2019 the Donation module has been evaluated with an average of 9.4/10, Transplantation 8.9/10, Management 8.9/10, Tissue Banking 8.9/10, IS 9.5/10 considering theoretical, practical sessions and course organization. In 2020-21 the evaluation was 9.2/10, 9.6/10, 9.2/10, 10/10, 9.2/10 taking into consideration the theoretical part, live sessions, and course organization. Comparative results indicate slight difference in the values, demonstrating stability despite the difficulties caused by the pandemic.

**Conclusions:** In the face of changes and restrictions caused by the pandemic the inclusion of new technologies has been essential to keep offering high quality international educational programs. Further exploring of technologies may also improve efficiency.
Pregnancies Fathered by Transplant Recipients

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The purpose of this study was to analyze 1408 pregnancy outcomes fathered by 875 male solid organ transplant recipients including exposure to mycophenolic acid products (MPA) and sirolimus. Data were collected by the Transplant Pregnancy Registry International (TPRI) via telephone interviews, online questionnaires, and review of medical records. Overall pregnancy outcomes fathered by transplant recipients are similar to the general US population (Table).

TPRI Fathered Pregnancies

Of the total fathered pregnancy experience, there were 333 outcomes with exposure to MPA. Outcomes included 297 (89%) live births, 33 (9.9%) miscarriages, 2 stillbirths and 1 ectopic pregnancy. Among the live births there were 11 birth defects reported (3.7%) and included: undescended testicle (n=2), tongue tied, pyloric stenosis, club foot, ureteral reflux, ventricular septal defect, Klinefelter’s syndrome, Prader-Willi syndrome, Down’s syndrome, and diaphragmatic hernia (neonatal death).

Although male fertility has been reported to be decreased in males maintained on sirolimus, there are 29 fathered pregnancies resulting in 28 live births with 1 birth defect (ureteral stricture) and 1 miscarriage with exposure to sirolimus.

Conclusions: The outcomes of pregnancies fathered by male transplant recipients are comparable to the general population and there is no evidence that male recipients need to avoid MPA when considering fathering a pregnancy. Data regarding sirolimus remains limited, however, to date increased risks for pregnancies fathered while taking sirolimus have not appeared. All transplant centers should encourage their recipients to participate in the TPRI.

Pregnancies Fathered by Transplant Recipients

<table>
<thead>
<tr>
<th>Organ(s) Recipients</th>
<th>Pregnanacies/Outcomes*</th>
<th>MPA exposure</th>
<th>Live births</th>
<th>Mean gestational age (weeks)</th>
<th>Mean birthweight (g)</th>
<th>Birth Defects</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>632</td>
<td>997/1019</td>
<td>21%</td>
<td>92%</td>
<td>39 ± 2.3</td>
<td>3357 ± 596</td>
<td>3.5%</td>
</tr>
<tr>
<td>Heart</td>
<td>121</td>
<td>181/188</td>
<td>23%</td>
<td>89%</td>
<td>38.7 ± 2.4</td>
<td>3351 ± 659</td>
<td>3.6%</td>
</tr>
<tr>
<td>Liver</td>
<td>87</td>
<td>148/155</td>
<td>22%</td>
<td>87%</td>
<td>39 ± 1.9</td>
<td>3318 ± 606</td>
<td>3.8%</td>
</tr>
<tr>
<td>Kidney</td>
<td>35</td>
<td>44/46</td>
<td>40%</td>
<td>91%</td>
<td>38.7 ± 2.4</td>
<td>3321 ± 589</td>
<td>2.4%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>39</td>
<td>3389</td>
<td>4-6%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*includes twins, triplets

TTS/ILTS Paired Transplant Center Program: Two Years of Clinical and Academic Advancements

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Introduction: The Paired Transplant Center Program is a TTS/ILTS initiative to expand worldwide surgical capacity of Liver Transplantation (LT). Hepatocellular carcinoma, HBV and HCV rates in Mongolia are among the highest in the world, for this reason, it is imperative to increase surgical capacity in this region. Our LT team (Supporting Center - SC) and our counterparts in Mongolia (Emerging Center - EC) through collaborations in a university-based academic Center for Global Surgery were accepted for the Paired Transplant Centers Program award in 2020. We aim to report on the academic and clinical advancements of our alliance.

Methods: This is a descriptive study to report the first 2 years of our partnership; We have organized online multidisciplinary lectures of selected LT topics with speakers from SC, EC, and international LT leaders. LT and related clinical protocols and guidelines are discussed during these meetings, allowing tilateral knowledge exchange. Research sessions include group review of abstracts and manuscripts from both teams. We also surveyed the participants of our group to obtain feedback about our past collaborations and future expectations of our projects.

Results: Our group consists of a multidisciplinary team of 30 participants (SC=17, EC=13). We had 27 lectures on diverse LT topics, and we participated in over 14 LT international meetings including ILTS and TTS. We have submitted 2 manuscripts, presented 4 abstracts and received support to sponsor 1 research scholar. We reviewed and discussed bilateral protocols on immunosuppression, donor selection and follow-up, biliary complications, COVID-19 vaccination and perioperative care. Twenty-two (73% response rate) participants of our group answered the survey, 77% agrees that the TTS/ILTS Paired Transplant Center Program has contributed to their academic growth by providing new ideas for quality improvement and research projects, 68% agree that the collaboration has increased their knowledge in transplant and help them provide better care for their patients 72%, 81% think they would benefit from discussing pediatric transplantation topics and clinical cases and 26% and 66% respectively see language/translation and other clinical and academic duties as a challenge for our meetings.

Conclusion: Our results show that it is feasible to have clinical and academic advancements through online efforts that ultimately impact bilateral patient care. Partnering with ECs and participating together in international studies helps expand their network for further independent collaborations. COVID-19 has limited in-person collaborations; however, telehealth platforms have been a useful and affordable tool for international collaboration among LT centers around the world.
Objectives: To analyze the impact of this program on the accessibility of the waiting list for kidney transplant and for the kidney transplant itself in the region. Demonstrate the social equity achieved in access to kidney transplant (KT) and in the admission to the waiting list (WL).

Methodology: We used ORESI (an excel statistical system) to collect and analyze data before and after the creation of the renal transplant team.

Results: In Argentina the population with Terminal Kidney Disease (TKD) is of 28821 patients, the WL for KT is of 5088 patients. Misiones has a population of 1284760 inhabitants, 667 of whom have TKD. The population with TKD has a growth rate that shows a sustained increase of 4.09% annual average since 2013. Diabetic nephropathy is the main cause. The Madariaga Hospital Transplant Service (Posadas, Misiones) has been created in 2018 with the purpose of ensuring the opportunity for KT in an equitable manner for the population of the province and guaranteeing equity to all patients in the province who need to enter WL and receive a transplant in a timely manner. Thanks to the development of this new transplant center, it has been possible to increase significantly the transplant rate in the province of Misiones. With the creation of the public transplant program. Three variables have multiplied exponentially: 1- The number of patients on the WL 2- The number of transplants 3- The rate of organ and tissue donation in the hospitals of the country. Until 2018 there was a strong rising curve. However, since 2018 there has been a trend towards a flattening of this curve.

Discussion: The political decision to form this team in a highly complex hospital is to guarantee health care to the entire population of the province regardless of their health insurance. The equity of this program is due to the response provided to the entire province in a homogeneous way. Supported by the hospital dialysis centers all around the province, coordinating studies for admission to WL, and coordinating the patient transfers from all over the province. Despite the rising incidence of the KT population, having been able to increase the WL and the 74 transplants performed so far have achieved a flattening in the historical upward curve of HD patients year after year. We therefore believe that this data demonstrates effectiveness in the process. Observing that the trend begins to change and seeing the projection of it over time speaks of a more encouraging future for the entire population, prioritizing the most in need patients.

Introduction: This paper analyzes the results of the impact of the Kidney Transplant Program in a Public Hospital in the province of Misiones, Argentina. The population are patients who have been indicated a kidney transplant without medical insurance coverage.

Accessibility to Renal Kidney Transplant. Equity of the Public System. Misiones, Argentina

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Introduction: Comprehensive education is needed of all doctors who might one day be relied upon to identify, refer, and manage potential donors while comforting a grieving family. Online education platforms offer a method of teaching medical professionals and the public on a large scale about deceased organ donation best practices. Developing countries have insufficient resources to educate health professionals in the skills to identify and support potential organ donors and their families. We describe the 5-year demographic and geographic profile and perceptions of participants who completed a MOOC on organ donation offered by an African university via a global platform.

Methods: A 5-year review of the massive open online course Organ Donation: From Death to Life since its launch is July 2017 was done using the Coursera analytics platform. Local uptake in South African Universities was also reviewed.

Conclusion: Online education resources on aspects around organ donation are well received. Local champions are needed at universities to run such a course and ensure we educate all our graduates on this important topic.

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345.6

A Quality Analysis of Donor Nephrectomy-Related Information on YOUTUBE; Education or Misinformation?

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Background: In 2019 approximately 7000 live donor nephrectomies and living donor kidney transplants were performed in the United States, accounting for 29.3% of all kidney transplants nationally. There remains an urgent need to increase living kidney donation to help mitigate the high demand for waitlisted kidney failure patients. Potential kidney donors can readily access social media, particularly YouTube, to gain basic knowledge about live donor nephrectomy surgical procedures. YouTube is an open source platform where anyone can upload videos about any topic without peer review or quality control, and is frequently used for the dissemination of health education¹. This calls into question the credibility of YouTube videos as a source of patient education for potential live kidney donors. This study aims to assess the quality and accuracy of information regarding live donor nephrectomy on YouTube.

Methods: A YouTube search was performed using the keywords “donor nephrectomy” and “kidney transplant”. The top 20 videos of the “Donor Nephrectomy” search result, and all videos with over 10,000 views from the search result “Kidney Transplant” were assessed for eligibility criteria. Two validated tools for evaluating health information, the DISCERN² and PEMAT-A/V³ tools, were utilized by two reviewers to assess YouTube video information quality, understandability, and actionability. The scores from the two reviewers were compared using interrater reliability to verify consistency of scoring. Data on source and video characteristics, presence of physician in video, and clinical mention of information related to donor nephrectomy were collected.

Results: A total of 53 of 57 screened videos were included in this study with 4 videos being excluded for not being primarily in English language. The number of views ranged from 9.46 million to 590, with a mean of 719,414. 33 (62.3%) of the videos were identified as promotional and included information on a specific practice, company, or health corporation. A medical doctor was present in 28 (52.8%) videos, 15 (28.3%) videos mentioned a surgical approach of any kind (open, vs laparoscopic vs robot assisted), and 8 (15.1%) videos mentioned potential acute or chronic complications/risks associated with live donor nephrectomy or living kidney donation. The mean (SD) DISCERN score was 23.3 (± 8.3), and the mean (SD) PEMAT-AV Understandability and Actionability scores of 41.7% (±17.5) and 8.2% (±22.9%), respectively.

Conclusions: Information on living donor nephrectomies is prevalent on YouTube. Our assessment using quality measures of selected videos illustrates substantial misinformation on living donor nephrectomies. YouTube has the potential to be a source of reliable and accurate information on living donor nephrectomies and donation.
Nutritional Diagnosis in Chronic Intestinal Failure Patients: GLIM Criteria vs Subjective Global Assessment

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Introduction: Parenteral Nutrition (PN) is the main support in Chronic Intestinal Failure (CIF) patients. As part of their regular evaluation, nutritional assessment is usually done through Subjective Global Assessment (SGA). The Global Leadership Initiative on Malnutrition (GLIM) developed phenotypic and etiologic criteria for assessing and grading malnutrition. The aims of this study were to compare these tools in nutritional assessment of CIF patients and determine the severity of malnutrition according to GLIM’s phenotypic criteria.

Methods: From June 2019 through December 2021 a retrospective analysis was conducted. All patients included had CIF diagnosis. Malnutrition was evaluated using SGA and GLIM criteria at the first office visit, while the degree of malnutrition was assessed according to phenotypic criteria. Descriptive, bivariate, multiple logistic regression and ROC analysis were performed.

Results: Seventy adult patients with CIF were included. Forty-two (60%) had short bowel syndrome. Mean age was 47.76 years and 51.4% were female. Nutritional status using SGA showed 40% patients well nourished, 27% moderately or suspected of being malnourished, and 33% severely malnourished. When using GLIM criteria, 60 patients (86%) presented at least 1 phenotypic criteria of malnutrition. In terms of etiologic criteria all patients had reduced food intake and/or impaired absorption or food assimilation. When grading malnutrition status 53% of patients had moderate and 33% severe malnutrition. The ROC analysis showed an area under the curve of 0.92 when SGA was analyzed and 0.86 for GLIM criteria (p = 0.98). (Figures 1 and 2)

Conclusion: Nutritional assessment in CIF patients is mandatory to improve malnutrition, if present. In this study GLIM criteria showed a higher percentage of patients with malnutrition, but when comparing ROC analyses not statically difference between SGA/GLIM was shown.

Professional Employment in Patients on Ventricular Assist Device Support – A Multi-Center Prevalence Study

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Background: Ventricular assist device (VAD) implantation aims to support end-stage heart failure patients for the long-term. For patients in productive age ranges, return to an active and productive work life can be seen as a surrogate marker for functional recovery, and psychosocial re-integration. This study aimed to assess professional employment, explore determinants, and the impact of adverse events on professional employment in stable outpatients on ongoing assist device support.

Methods: A national, multi-center study considered rates of professional employment and its relation to sociodemographic (age, gender, education, family), psychosocial (anxiety, depression, quality of life (QoL), and clinical adverse (thromboembolic, bleeding, driveline infection) outcomes in a large sample of 375 stable outpatients on ongoing VAD support. Valid patient-reported outcome measures were administered (WPI, KCCQ, HADS). Retirement age for women (<60yrs), and men (<65yrs) was considered.

Results: The overall sample consisted of 14% (n=53) female patients, mean age for the entire sample being 55±11years, mean time post-implant was 18±11mths, and ranged from 3-36mths. A minority of 15.15% (n=35; 95% CI 10.9-20.6) of the sample were full- or half-time employed. 52.3% (n=196) reported to be unemployed or retired illness-related, and 37.1% (n=139) were retired age-related. For the majority of those working the implant reason was bridge to transplantation 82.9% (n=29), and six patients were bridged to recovery. A regression model after variable selection (R2 Tjur 0.189) revealed younger age (OR 0.95; 95% CI 0.91-0.98; p=0.005), and higher education (OR 3.05; 95% CI 1.72-5.69; p<0.001) to support professional employment. Working patients reported on higher QoL using the KCCQ overall sum-score (OR 1.04; 96% CI 1.01-1.07; p=0.007), and the odds for those working was 2.18 (95% CI 0.89-5.41; p=0.08) indicating no significant relation for working and having had a history of one or more adverse events.

Conclusions: In this national sample, professional employment rates in patients on ongoing VAD support were rather small; however, those employed perceived better overall QoL. Professional employment was not significantly related to clinical adverse events relevant to this population. Future clinical strategies need to be initiated to support psychosocial re-integration in terms of professional employment for patients on VAD support being in the respective age ranges, which may increase patients’ overall QoL perceptions.
Keeping Up With Psychosocial Predictors of Outcomes in Solid Organ Transplantation: A User Friendly Interface To Identify, Organize and Facilitate Access to Empirical Data

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Introduction: Psychosocial factors in solid organ transplantation have been identified as predictors of transplant outcomes such as morbidity, mortality and quality of life. Given the scarcity of available organs, systematic identification of psychosocial factors affecting outcomes is crucial for determining patient suitability for transplant, as well as reducing the risk of post-transplant complications via targeted interventions. Hundreds of individual studies and dozens of meta-analyses have quantified the impact of psychosocial variables on post-transplant outcomes. Sourcing this data, interpreting it, and systematically applying it to within transplant settings is challenging due to the sheer amount of information available and lack of a system for organizing findings. Consequently, it is difficult to rigorously apply these findings to decision making for transplant suitability and patient care. The current study represents a step towards identifying, organizing and facilitating access to empirical data for the betterment of decision making and optimizing care.

Method: The study involved a systematic review of meta-analyses and systematic reviews. Electronic searches were performed using PubMed, Medline OVID, PsyCINFO and Web of Science. Inclusion criteria included systematic reviews and meta-analyses in English, adult population of transplant recipients, and inclusion of psychosocial outcomes.

Results: Twenty-six studies met criteria for inclusion, 16 of them were systematic reviews and 10 meta-analyses. Studies included 193 data points (17 heart, 27 kidney, 89 liver, 19 lung and 41 multiple organs). Predictor variables included 26 medical (e.g., late acute rejection); 27 mortality/survival; 87 substance use (e.g., high risk alcohol use); 20 psychological (e.g., PTSD, anxiety); 25 social (e.g., social support, marital status); 57 substance use (e.g., alcohol dependence); 8 vocational (e.g., employment status). Outcome variables included 26 medical (e.g., late acute rejection); 27 mortality/survival; 87 substance use (e.g., high risk alcohol use); 20 psychological (e.g., PTSD, anxiety); 8 quality of life; 18 behavioural (e.g., medication adherence) and 7 miscellaneous. The data have been organized in user-friendly spreadsheets that allow the user to look for the information by organ, risk factors and outcomes.

Conclusion: The goal of this study was to create a user-friendly interface to determine the impact of psychosocial predictors on post-transplant outcomes based on empirical data. As newer, appropriate studies arise they will be added to maintain an up-to-date interface. This will assist informed decision-making regarding transplant candidacy and guide interventions both pre and post-transplant to optimize outcomes.
International Collaborative Project to Set-up Deceased Organ Donation System in United Arabic Emirates (UAE): Preliminary Data

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Introduction: World Health Organization advocates for the development of self-sufficiency in donation and transplantation in all countries. In 2017, UAE initiated its Organ Deceased Donation (ODD) program, after the UAE Ministry of Health and Prevention issued the Decree number 550 on declaration of death, covering brain death diagnosis. It represented a start point to implement the ODD program in the area. Evolution of the UAE deceased donation program is represented in Figure 1. Donation & Transplantation Institute (DTI) is a non-profit organization that supports international entities to design and develop programs in the field of organ donation and transplantation. Since September 2021, Abu Dhabi Health Services Company (SEHA) and DTI are cooperating to define and implement an ODD program considering aspects such as consultancy, education, quality, innovation, and research.

Objective: The objective of this study is to describe the achievements after the implementation of ODD program in the UAE.

Methodology: 20 hospitals affiliated to the Organ Donation and Tissue Center (ODTC) participated in the study as well as Transplant Procurement Managers (TPM). TPMs have been involved closely with donor hospitals to build relationships and implement practices to facilitate organ donation, ensuring all donation opportunities are preserved, Hospital Development methodology. In order to train and provide experience to local professionals, capacity development initiatives such as workshops, conferences and other events have been performed by the hand of governmental endorsement.

Results: Updated standard operating procedures (SOPs) and clinical guidelines have been established in the UAE, organ donation evolution from September to December 2021 is represented in Figure 2.

□ Possible: A patient with a devastating brain injury or lesion or a patient with circulatory failure and apparently medically suitable for organ donation.

□ Potential: A person whose clinical condition is suspected to fulfill brain death criteria.

□ Elegible: A medically suitable person who has been declared dead based on neurologic criteria as stipulated by the law of the relevant jurisdiction.

□ Actual: A consented eligible donor: From whom an operative incision was made with the intent of organ recovery for the purpose of transplantation. Or from whom at least one organ was recovered for the purpose of transplantation.

□ Utilized: An actual donor from whom at least one organ was transplanted.

Conclusions: Preliminary results show a major increase (433%) in the number of actual donors after the implementation of “Hospital Development” methodologies, compared with 2020 activity. Main barriers to be faced are unbalanced healthcare infrastructure and coverage, complex healthcare policies, and shortage of trained professionals. Regarding the population, low engagement due to multi-religious and cultural facts and insufficient awareness are the main challenges.
345.12

Virtual Education and Support Program for Transplant Patients and Caregivers During COVID

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Introduction: In response to the COVID-19 pandemic transplant teams began restricting in-person patient (Pt) visits and clinical interactions. Many in-person appointments became virtual and Pts and caregivers (CG) had reduced opportunities to interact in-person with other Pts in hospital waiting rooms, clinic services, and hospital-based support groups. Our organization, an affiliate of the local Organ Procurement Organization (OPO), is a healthcare hospitality house specializing in support of transplant families. In addition to lodging and other services, we develop education and support programs for transplant Pts and CGs. Early in the pandemic we began to examine programs to address opportunities for providing uninterrupted supportive services to transplant families.

Method: In early 2020 we began to identify topics of interest for transplant Pts and CGs such as post-transplant medication, nutrition and diabetes, transplant-specific COVID updates, and mental health. All virtual education programs were presented by transplant professionals and experts. Programs were presented through an online webinar platform and registration was open for any transplant Pt, CG, or professional throughout the US and internationally at no expense.

Results: Between 2020-2021 we offered 25 virtual education programs with 2,237 participating devices (non-unique users), representing participants from 44 US states and 8 countries. Approximately 75% of registrants were transplant Pts, 15% transplant professionals, and 10% transplant CGs. An evaluation was provided to registrants following each program and 645 evaluations were completed (29%). The evaluation was comprised of Likert scale and qualitative questions. Participants provided a rating of the program from poor to excellent (1-5) and the average response rating was 4.48. The following questions were rated strongly disagree to strongly agree (1-4); the content was presented effectively with an average rating of 3.73, questions were answered satisfactorily with an average rating of 3.80, and new knowledge was gained with an average rating of 3.58. One responded, “As a long-time recipient, I am still eager to learn more not only to benefit me but to help others on their journey.” Another responded, “I appreciate this kind of contact with professionals that really care about our health…”

Conclusion: Many transplant Pts and CGs were reminded of the additional physical and social precautions necessary for their health and safety throughout COVID. Virtual education and support are vital for Pts and CGs to receive important information about their health as well as to enable development of support networks with others similarly situated. Based on the consistently high participation rates and evaluation results, it is reasonable to conclude that Pts and CGs find value in these programs and committing to the development and delivery of accessible, low-cost programs are important for Pts and their CGs throughout their journey.

TD Grant.

346.1

Hepatitis B virus Suppression Predicts Better Recurrencefree Survivals in Liver Transplant Patients With Hepatocellular Carcinoma

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Introduction: High serum load of hepatitis B virus (HBV) deoxyribonucleic acid (DNA) is known to be a strong risk factor of hepatocellular carcinoma (HCC) development. The aim of study was to investigate the predictive role of HBV DNA levels in recurrence of HCC after liver transplantation (LT).

Methods: From June 2006 to May 2020, 729 recipients underwent LT for HBV-related HCC in Seoul National University Hospital. The risk factors for HCC recurrence after LT were analyzed including serum HBV DNA load.

Results: Recurrence-free survival at 1, 3, 5, and 10 years were 99.6%, 98%, 95.1%, and 87.8%, respectively. Detectable HBV DNA level (higher than 10 IU/mL) before transplant was significant predictors of HCC recurrence in univariate analysis (P=0.027). Further subgroup analysis was performed to demonstrate the significance of HBV DNA level according to the risk of HCC recurrence. Based on the score of the predicted survival after liver transplantation for HCC (SALT), patients were divided in three groups. In high risk group of recurrence with SALT score more than 2.44, detectable HBV DNA level were significantly associated with recurrence free survival (57.9 % vs. 78.7 %, P<0.0001).

Conclusion: There is a close relationship between HBV DNA level and HCC recurrence after transplant. High HBV DNA levels before transplant are associated with HCC recurrence after transplant, especially in high recurrence risk group.
Preoperative Neutrophil and Platelet-To-Lymphocyte Ratio As Predictors of Mortality and Surgical Related Complications After Liver Transplantation

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Introduction: Liver transplantation (LT) is considered the only definitive treatment in patients with end-stage liver disease (ESLD). Nowadays, the 5-year overall survival (OS) after LT is 75%–85%. In addition, short-term mortality has decreased due to better perioperative care, advancements in operative techniques, as well as changes in patient selection. Despite these improvements, a subset of patients still dies within the first year after LT. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been recently reported as simple and useful markers of various inflammatory changes and are calculated based on complete blood count data. It has been suggested that both parameters in the acute phase of LT are prognostic factors for early post-transplant survival.

Method: We conducted a retrospective and analytic study. Among 410 LT recipients between January 2013 and February 2022 who were operated at the HPB surgery and liver transplant department of the Hospital de Alta Complejidad “El Cruce”, we selected 120 patients after simple random sampling. Patients’ demographic data, cirrhosis etiology, model for end-stage liver disease (MELD) scores, and hematological parameters were analyzed. Latest hematological parameters prior to surgery were recorded. NLR and PLR values were calculated based on the measured hematological parameters. Time and incidence of postoperative complications were analyzed. Fisher exact test, Mann–Whitney U test and Students T-test were used when appropriate. Two-sided p value equal or less than 0.05 was considered to indicate statistical significance with a confidence interval of 95%. All analyses were conducted using MedCalc version 20.027 (https://www.medcalc.org/).

Results: The mean age of the 120 patients included in the study was 58.7 ± 7.04 years; 66.67% were male. All patients received deceased donor liver transplantation. The most common indication for LT was liver cirrhosis due to hepatitis C virus (HCV) (30%) followed by alcoholic liver cirrhosis (26.67%) (table 1). The mean MELD score was found to be 24.85 ± 6.67. 23 out of 120 patients died after LT (19.16%). 5 patients (4.16%) had non-resectable NET liver metastasis confined to the liver (8 whole grafts and 2 splits). After the LT, patients continued receiving somatostatin analogues and/or TACE. Seven patients (58%) were given additional MELD points and after a median of 3 months (range 1-17) 10 patients (91%) received a cadaveric liver (8 whole grafts and 2 splits). After the LT, patients continued receiving somatostatin analogues (n=8) and everolimus (n=1). As post-transplant complication, 2 patients presented graft rejection, 1 pseudoaneurysm of left hepatic artery and 1 ischemic cholangiopathy. Disease free survival was of 91%, 57% and 43% after 1-, 3- and 5-years post-LT (Fig. 1). Five patients had disease recurrence, 2 were treated with surgery, one with cisplatin and 1 underwent several medical treatments. Patient survival at 1, 3 and 5 years was of 91%, 78% and 78%, respectively (Fig. 2).

Conclusion: Preoperative NLR and PLR were not found useful to predict mortality after OLT in our series. However, they may be of value to anticipate poor prognosis or major incidence of complications in patients undergoing OLT. With this simple indices, high-risk patients can be identified and preventive measures can be taken.

Table 1: Demographic data of the sample (N = 120)

<table>
<thead>
<tr>
<th>Sex (male)</th>
<th>Age</th>
<th>Main etiology of liver disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 (66.67%)</td>
<td>58.73 ± 7.04</td>
<td>25 (20.83%)</td>
</tr>
<tr>
<td>Male</td>
<td>5.17%</td>
<td>Hepatitis C virus</td>
</tr>
<tr>
<td>4.16%</td>
<td>12.5%</td>
<td>Alcohol liver cirrhosis</td>
</tr>
<tr>
<td>3.33%</td>
<td>9.17%</td>
<td>Others</td>
</tr>
<tr>
<td>4.16%</td>
<td>9.17%</td>
<td>Primary biliary cirrhosis</td>
</tr>
<tr>
<td>4.16%</td>
<td>10.83%</td>
<td>NASH</td>
</tr>
<tr>
<td>4.16%</td>
<td>9.17%</td>
<td>Autoimmune hepatitis</td>
</tr>
<tr>
<td>4.16%</td>
<td>9.17%</td>
<td>Hepatitis B virus</td>
</tr>
<tr>
<td>4.16%</td>
<td>9.17%</td>
<td>Secondary biliary cirrhosis</td>
</tr>
<tr>
<td>4.16%</td>
<td>9.17%</td>
<td>Primary sclerosing cholangitis</td>
</tr>
<tr>
<td>4.16%</td>
<td>9.17%</td>
<td>Hemosiderosis</td>
</tr>
<tr>
<td>4.16%</td>
<td>9.17%</td>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>MELD</td>
<td>24.85 ± 6.67</td>
<td>12-40</td>
</tr>
<tr>
<td>NLR</td>
<td>3.54 ± 4.08</td>
<td>0.59-39.5</td>
</tr>
<tr>
<td>PLR</td>
<td>80.73 ± 50.59</td>
<td>14.62-309.5</td>
</tr>
</tbody>
</table>

Liver Transplantation for Metastatic Neuroendocrine Tumor in Argentina: Outcomes From a Multicenter Study

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Introduction: Neuroendocrine tumors (NET) most common site of metastases is the liver and they usually present themselves as multiple, bilateral masses. For these patients, when the lesions are unresectable, the orthotopic liver transplantation (LT) presents a viable treatment option.

Patients and Method: Retrospective study of patients who underwent liver transplant due to NET metastases between 2007 and 2022 in 3 centers in Argentina. Patients were identified from existing databases at each unit, sent in an excel form and then put altogether in an IBM SPSS data sheet which was used to perform statistical analyses. Variables included were: age, sex, type of primary tumor, time of diagnosis of the liver metastases, type of graft, place of recurrence and patient survival.

Results: Eleven patients received a LT due to inresectable NET metastases, 7 of them (64%) were women with a mean age of 49 ± 8 years old. In 8 patients (73%) the primary tumor was located in the small bowel and 10 cases (91%) were diagnosed with synchronous metastases. As part of the primary tumor resection, 4 enterectomies were performed (36%), 4 right hemicolecotomies (36%) and 3 distal pancreatectomies with splenic preservation (8%). Afterwards, 8 patients (73%) were given somatostatin analogues and 1 everolimus. In 4 patients (36%), alternative treatments were employed to try to treat de liver metastases, including surgery, radiofrequency ablation and/or TACE. Seven patients (64%) were given additional MELD points and after a median of 3 months (range 1-17) 10 patients (91%) received a cadaveric liver (8 whole grafts and 2 splits). After the LT, patients continued receiving somatostatin analogues (n=8) and everolimus (n=1). As post-transplant complication, 2 patients presented graft rejection, 1 pseudoaneurysm of left hepatic artery and 1 ischemic cholangiopathy. Disease free survival was of 91%, 57% and 43% after 1-, 3- and 5-years post-LT (Fig. 1). Five patients had disease recurrence, 2 were treated with surgery, one with cisplatin and 1 underwent several medical treatments. Patient survival at 1, 3 and 5 years was of 91%, 78% and 78%, respectively (Fig. 2).

Discussion: Non-resectable NET liver metastasis confined to the liver is an accepted indication for liver transplantation. We have shown that patient’s survival is similar to the median survival of those who received a liver graft due to HCC being (in both cases) essential the correct selection of patients who will undergo the LT.
### Abstracts

**346.4**

**Outcomes of Liver Transplantation at an Argentinian Program With 25 Years of Experience**

Dario N Teran,1 Maria F Fernandez,1 Leonardo Montes,1 Victoria Atencio2, Pablo A Farinelli1, Diego A Ramisch1, Guillermo Orce5, Francisco Klein1, Silvina Yantorno2, Pablo Barros Schelotto1, Valeria Descalzi2, Gabriel E Gonzalez1.

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**Introduction:** Liver transplant (LTx) is the treatment of choice for patients with end-stage liver disease. Twenty-five years after the program was started, several regulatory changes and reviewed guidelines, like the introduction of the MELD score, the prioritization criteria for HCC patients, and the effective treatment for HCV have impact transplant applicability and long term results. Different centers around the world have reported one year survivals close to 90% and 75% at 5 years. The aim of this study is to report long term outcomes of patients undergoing LTx at our center.

**Material and methods:** Retrospective analysis of patients >18 years old who received LTx or re-transplant (re-Tx) between June 1995 and March 2022. Donor’s and recipient’s clinical variables, including graft and patient were analyzed. Statistical analysis was performed with SPSS version 25.0.

**Results:** A total 1246 LTx were performed during the period of study; 1001 (80%) were adults, 580 (58%) were male, mean age was 58 ± 13 years; 918 (92%) were primary transplants and 83 (8%) re--Tx. The indications for LTx were: 767(77%) Cirrhosis, 86 (9%) acute liver failure, 83(8%) re-Tx and 65 (6%) others. If we divide them by type of transplant: 933 (93%) were liver, 60 (6%) combined liver-kidney and others 1% (3 combined intestinal-liver, 2 liver-heart, 2 multivisceral and 1 liver-lung). Nine hundred and thirty-eight (93.7%) LTx were performed with cadaveric donor; 60 (6%) with living donor, 3 (0.3%) were part of domino liver transplant. Among the group of patients that received cadaveric grafts, 896 (95%) were whole liver and 42 partial grafts. Table 1 shows the main causes of primary LTx divided by periods. Eighty three cases (8%) were re-Tx: 21 due to ductopenic rejection (2%), 17 had arterial thrombosis (1.7%), 15 disease recurrence (1.5%), 9 ischemic cholangiopathy (1%), 6 PNF (0.6%), 3 (0.3%) graft dysfunction, others: 0.9%.

**Conclusion:** Alcoholic liver disease, HCC and NASH had significantly increased in our second period of evaluation. According to current published international results, our center presents’ comparable results to other local, regional and international centers.
Reno-Portal Anastomosis in Liver Transplantation With Complex Portal Vein Thrombosis. Results of a Single Center Experience in Mexico

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Introduction: Portal vein thrombosis has been reported in liver cirrhosis (1-28%) and is not an uncommon scenario in patients in the waiting list for a liver transplant. Portal inflow is extremely important for successful revascularization of the liver graft and resolution of portal hypertension. Complex portal vein thrombosis represents a challenge in liver transplant surgery. Reno-portal anastomosis, first described in 1997, is a technique used in selected patients for portal reconstruction in complex portal vein thrombosis with splenorenal shunt, however it is not extensively reported (around 66 cases in total). The aim of this study is to describe and analyze the outcomes of patients with a reno-portal anastomosis at our institution.

Method: We reviewed patients that underwent liver transplantation at our institution, from 2018 to 2021. Those who underwent reno-portal anastomosis were included. Descriptive analysis was performed. Variables were extracted from our prospective database and analyzed with SPSS Version 22.0.

Results: Of 168 liver transplants, 7 allografts (4.2%) were primarily revascularized with a reno-portal anastomosis. All of them had portal thrombosis Yerdel IV and a significant spleno-renal shunt detected preoperatively with CT. 6 patients (85.7%) were male. The median age was 49 (30-66) years and median BMI was 27 (22-34.2). Table 1 summarizes the more important variables studied.

Complications were present in 5 patients (71.4%). Major complications (Clavien-Dindo > 3=1) were present in 3 patients (42.8%). 4 patients (57.1%) developed acute kidney injury however, all of them resolved within the first 48 hours and did not require hemodialysis. 2 patients (28.6%) developed ascites postoperatively, in one the portal reconstruction was thrombosed and in the other the portal inflow was not adequate. Only one patient (14.3%) presented vascular graft thrombosis and required reintervention. 2 patients (28.6%) died within 90 days: one of them despite reno-portal anastomosis and normal liver function. The median follow up was 25 months.

Conclusion: Reno-portal anastomosis is a feasible option in patients with complex portal vein thrombosis and the presence of a significant splenorenal shunt, achieving in most cases an adequate portal inflow and resolution of portal hypertension, with low rate of thrombosis of the reconstruction. Our institute performs the largest number of liver transplants in Mexico. We experienced an evolution through the years, increasing our capacity to do more complicated procedures with acceptable results.
Liver Biopsy in a Clinic Set Up

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Purpose: The aims of this performance improvement project include the following:
□To start doing liver biopsy in the clinic set up.
□To increase the liver biopsy being performed in the hospital for potential donor heptatectomy.
□To standardize practice of liver biopsy being done across the hospital either in OR, Interventional Radiology or the clinic set up (Level 8A – Adult Liver Clinic).
□To facilitate accommodation of having more potential donors being screened.

Method: The performance improvement project was explained to the nurses and staff are being selected to be part of the initial team for liver biopsy. Currently liver biopsy for potential donor hepatectomy is performed using OR (Operating Room) slots thru DSU (Day Surgical Unit). Several collaborative meetings were held involving the stake holders; Head of the Hepatology Medical Drs, Quality team, Program Director, Assistant Chief of Executive Nursing Department, Liver Clinic HN, OR HN, DSU HN, Informatics, Infection Control team and Liver team Clinical Instructor. In regards to those meetings held, suggestions and recommendations are laid down, and plans on how to execute the flow of liver biopsy has been properly scrutinized in accordance with the hospital policies and procedures. Selected staff nurses are required to be ACLS and Procedural Sedation qualified. Trainings and education are being conducted to make sure staff nurses are equipped with knowledge and skills to start the Liver biopsy in the clinic. Liver biopsy flow pathway was created and mock simulation was organized, in collaboration with every department involved. Some gaps and concerns are addressed.

Results: The PI project utilizing liver biopsy in the clinic started 2nd week September 2 cases per week and as to date we have 515 cases done. With those cases no major or serious complications has been documented. With a few minor complications were noted during liver biopsy such as hypotension and vasovagal effect. Otherwise all potential donors were being discharged safely. Potential donors were being taken cared of appropriately post liver biopsy.

Clinical relevance: The number of cases will surely helped the organization and skills to start the Liver biopsy in the clinic. Liver biopsy flow pathway was created and mock simulation was organized, in collaboration with every department involved. Some gaps and concerns are addressed.

Liver Fibrosis Measured by Magnetic Resonance Elastography Predicts Late Recurrence of HCC After Hepatic Resection

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Introduction: Hepatocellular carcinoma is one of the most common cancers in the world. The best curative treatment for hepatocellular carcinoma is liver resection. However, it has been known that there is a high possibility of recurrence if there is cirrhosis even after liver resection. Some studies recently explored the differences between early and late recurrence and investigated the risk factors for each type of recurrence. Predictive factors for early recurrence, i.e. recurrence within 24 months of surgery, are well established and are mainly tumor- and treatment related (i.e. tumor size, tumor number, presence of microsatellites, and vascular invasion). By contrast only poor data are available for the prediction of late recurrence, i.e. recurrence 24 months post-surgery, which is probably related to the evolution of the underlying chronic liver disease. Among the possible predictive factors for late HCC recurrence, the presence and the degree of portal hypertension (PH) could play an important role. In the last decade, several authors have tried to assess PH with non-invasive methods. In particular the role of liver stiffness have been investigated as non-invasive marker of PH and its complication. Generally, transient elastography (TE) used for liver stiffness measurement (LSM) for a long time. In addition to TE, magnetic resonance elastography (MRE) has emerged as another non-invasive method to evaluated liver fibrosis. MRE has advantages over TE including the acquisition of images that can be referred for LSM and a larger sampling area. Owing to these theoretical merits of MRE over TE, MRE provided significantly better performance in assessing liver fibrosis than TE in previous studies.

Method: Between January 2014 and December 2018, 603 patients underwent Hepatic resection (HR) for HCC. Among 603 patients, 245 patient checked MRE, but 5 cases had technical failure. We analyzed 241 patients. HCC recurrence was defined as the recent AASLD guidelines as early (if occurring <24 months) or late (if occurring >24 months). The follow-up protocol included a clinical assessment by physical examination, US and laboratory exams every 3 months. HCC recurrence was defined as early recurrence if there is cirrhosis even after liver resection. Some studies recently explored the differences between early and late recurrence and investigated the risk factors for each type of recurrence. Predictive factors for early recurrence, i.e. recurrence within 24 months of surgery, are well established and are mainly tumor- and treatment related (i.e. tumor size, tumor number, presence of microsatellites, and vascular invasion). By contrast only poor data are available for the prediction of late recurrence, i.e. recurrence 24 months post-surgery, which is probably related to the evolution of the underlying chronic liver disease. Among the possible predictive factors for late HCC recurrence, the presence and the degree of portal hypertension (PH) could play an important role. In the last decade, several authors have tried to assess PH with non-invasive methods. In particular the role of liver stiffness have been investigated as non-invasive marker of PH and its complication. Generally, transient elastography (TE) used for liver stiffness measurement (LSM) for a long time. In addition to TE, magnetic resonance elastography (MRE) has emerged as another non-invasive method to evaluated liver fibrosis. MRE has advantages over TE including the acquisition of images that can be referred for LSM and a larger sampling area. Owing to these theoretical merits of MRE over TE, MRE provided significantly better performance in assessing liver fibrosis than TE in previous studies.

Conclusion: Magnetic resonance elastography that measure liver fibrosis predict de novo recurrence after hepatic resection for hepatocellular carcinoma. So we consider liver transplantation in severe stiffness liver parenchyma.
Miami Protocol for Liver Deceased Donors After Circulatory Death: Increased 1-Year Overall Survival for Selected Patients

Phillepe Abreu1, Vighnesh Venkataramayi1, Juliano Riella1, Giselle Guerra1, Rafael Miyashiro1, Alfred Joseph Tector1, Akin Tekin1, Gennaro Selvaggi1, Rodrigo Vianna1.

Department of Transplantation Surgery, Jackson Memorial Hospital, University of Miami, Miami Transplant Institute, Miami, FL, United States.

Background: The use of deceased donors after circulatory death (DCD) for liver transplantation (LT) is still underutilized. It provides an acceptable solution to increase the organ donor pool without affecting outcomes. We analyzed data of DCD donors for LT in order to identify risk factors for graft and patient survival.

Methods: This was a retrospective cohort study using data reviewed by screening SRTR/UNOS of patients that underwent liver transplantation with DCD donor at the University of Miami, Jackson Memorial Hospital in Miami, FL from 2017 to 2019. Different surrogates were analyzed, including donor, recipient, procurement and transplant operation characteristics. The primary outcome was patient and graft survival. Continuous variables were analyzed using a 2-sided student t-test. Categorical variables were presented as frequencies and proportion and compared using chi-squared or Fisher’s exact test as appropriate. Univariable Cox proportional hazards models were fit in order to assess the impact of individual covariables on the instantaneous rate of events, with time-to-event analysis also being ascertained through Kaplan-Meier estimates.

Results: 54 cases were analyzed with a median MELD score of 18.5. Alcoholic cirrhosis was the most prevalent etiology for liver disease. There was 1 case with intra-hepatic biliary stricture, and 7 patients with anatomic strictures that required stenting. The 1-year survival rate following liver transplant using DCD donors was 90.7%. The total cold ischemic time (CIT) (HR 1.9, 95% CI 1.1-3.2) and diagnosis of rejection (HR 9, 95% CI 1.1-18.8) were statistically significant affecting graft failure. Estimated blood loss (EBL) (HR 1.1, 95% CI 1.1-1.2) was found to be statistically impacting overall survival rate.

Conclusion: DCD donors are excellent options to increase the availability of organs for patients waiting for a LT. CIT and EBL are the main predictors of poor outcomes and thus should be carefully taken into account when matching organs to recipients.

Unraveling the Stage-Shift of Acute Rejection in Renal Allografts

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Introduction: The lack of accuracy in current allograft monitoring methodologies for allograft monitoring underscores a critical unmet need for more accurate immunosurveillance to uncover the flux in alloimmunity. QSant – a non-invasive, urine based multi-analyte diagnostic test – was clinically validated to prognosticate injury, risk of evolution, and resolution of acute rejection. QScore—the composite score across measurements of DNA markers: the amount of cell-free DNA, fraction of methylated cDNA, protein and metabolic biomarkers in the QSant assay—enables this risk prognostication. This study now explores the clinical utility of QSant across the alloimmunity gradient of 32–100 for the early diagnosis of allograft injury and rejection.

Methods: Utilizing a large real-world dataset of contemporaneous kidney allograft biopsy and QSant data from 11 US kidney transplant centers, the QSant offers a dynamic view into the changing state of allograft injury and rejection in response to alterations in the patients’ immunosuppression regimen. First analysis included Q-Score distributions in the biopsy-paired validation (n = 162) and prediction (n = 91) data from the Yang cohort, which were collected between 2010 and 2018. Second was a new analysis of a real-world data (RWD) cohort, comprising of prospectively collected urine samples (n = 235).

Results: The RWD cohort (n = 235) of both adult and pediatric renal transplant patients demonstrated a spectrum across the Q-Score distribution. Specifically, 37.9% of the samples were enriched for immune quiescence (Q-Score < 32); the remaining 62.1% were enriched for the injury/rejection spectrum (Q-Score ≥ 32). The Qscore <32 classifies stable allograft recipients; Qscore between 32-55 exposes a state of alloimmunity flux; and the score between 55-100 provides advanced alloimmunity. Serial monitoring by QSant across a subset of 32 patients (RWD cohort,) over a period of two consecutive quarters (timepoints 1 and 2), captures the essence of the alloimmune injury gradient (n = 162) and prediction (n = 91) data from the Yang cohort, which were collected between 2010 and 2018. Second was a new analysis of a real-world data (RWD) cohort, comprising of prospectively collected urine samples (n = 235).

Conclusion: The observed alloimmunity flux suggested precision monitoring with QSant has the potential to differentiate higher-grade acute rejection episodes from sub-clinical rejection, thereby improving a transplant recipient’s quality of life.
Multiplexed Droplet Single-Cell Sequencing (Mux-Seq) of Normal and Transplant Kidney


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Maintenance of systemic homeostasis by kidney requires the coordinated response of diverse cell types. Use of single-cell RNA sequencing (scRNAseq) for patient samples remains fraught with difficulties. The ability to characterize immune and parenchymal cells during transplant rejection (some of which may be present at very small numbers due to injury) will be invaluable in defining transplant pathologies. Herein, we present feasibility data for multiplexing approach for droplet scRNAseq (Mux-Seq). Mux-Seq has the potential to minimize experimental batch biases and variations. Explant tissues from 6 normal and 2 transplant recipients after multiple rejection episodes leading to nephrectomy were pooled for Mux-Seq. Subsequently, a computational tool, Demuxlet was applied for demultiplexing the individual cells. Each sample was also applied individually in single microfluidic run (singleplex). We show that data from Mux-Seq correlated highly with singleplex (Pearson coefficient 0.982). Both are able to identify many known kidney cell types including immune cells. Trajectory analysis of proximal tubule and endothelial cells demonstrates separation between healthy and injured kidney from transplant explant suggesting various stages of differentiation. This study provides the technical groundwork for understanding the pathogenesis of alloimmune injury and host tissue response in transplant rejections leading to graft failure in clinical setting.

Transcriptomic Analysis Identifies a Tolerogenic Dendritic Cell Signature

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Introduction: Dendritic cells (DC) are central to regulating innate and adaptive immune responses. Strategies that modify DC function have provided new therapeutic opportunities in transplantation. Current pharmacological approaches can alter DC phenotype to induce tolerogenic DC (tolDC), a maturation-resistant DC subset capable of directing a regulatory immune response that are being explored in current clinical trials in transplantation. The classical phenotypic characterization of tolDC is limited to cell-surface marker expression and anti-inflammatory cytokine production, although these are not specific for current clinical trials. TolDC may be better defined using gene signatures, but there is no consensus definition regarding genotypic markers.

Methods: We address this shortcoming by analysing available transcriptomic data to yield an independent set of differentially expressed genes that characterize human tolDC. We have validated this transcriptomic signature and also explored gene differences according to the method of tolDC generation.

Results: We established a set of 53 genes that accurately described the human tolDC genotype. The dataset was also validated in three independent, publicly available tolDC RNAseq datasets. Further, we utilised single cell RNAseq to establish that DCs isolated from the liver appeared to be more correlated with tolDCs than any other organ.

Discussion: Our panel of 53 genes may serve to independently quantify the regulatory capacity of a tolDC prior to clinical trial administration. Our finding, that DCs isolated from the liver are more tolerogenic than other organs may provide reasoning for the decreased incidence of rejection and resistance to ischemic perfusion injury within the liver.
Gender Disparities in Liver Transplantation: Minority Women Suffer Greater Mortality on the Waitlist

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Background: Non-alcoholic steatohepatitis (NASH) is a rapidly-growing indication for liver transplantation (LT) in the West. Gender disparities in LT rates are well-established. We sought to analyze gender disparities amongst NASH patients with cirrhosis and their access to LT in a contemporary cohort.

Methods: We used data from scientific registry of transplant recipient to assess gender and ethnic differences in patients listed for LT. Adult patients transplanted from August 1997 to June 2021 were included. Inferential statistics were used to evaluate differences with univariate and multivariate comparisons. Regression modeling using a forward conditional approach was performed.

Results: During the study time period, we evaluated 12,844 LT for NASH cirrhosis. Women were transplanted at a lower rate (46.5% vs 53.5%; p<0.001) and at a higher MELD (23.8 vs 22.6; p<0.001) than men. Minority women were transplanted at a higher MELD (26.1 vs 23.1; p<0.001) than white women and minority men (26.1 vs 24.8; p=0.001). Furthermore, minority women with NASH have a lower BMI (32.2 vs 32.1; p=0.002) on the waitlist compared to white women but minority women with NASH have a higher mortality (21% vs 18%; p=0.006) on the waitlist compared to white women. Patient survival for women at 1, 3, and 5 years was 90.3%, 83.4%, and 77.3%, respectively, and graft survival was 95.9%, 94.4%, and 93.3%, respectively. By comparison, patient survival for men at 1, 3, and 5 years was 93.6%, 87.1%, and 80.3%, respectively and graft survival was 97.6%, 95.6%, and 93.8%, respectively. Minority women patient survival at 1, 3, and 5 years was 89.3%, 82.2%, and 76.0%, respectively. Minority women graft survival at 1, 3, and 5 years was 95.4%, 94.1%, and 92.2%, respectively. Non-minority women patient survival at 1, 3, and 5 years was 93.9%, 87.4%, and 79.2%, respectively. Non-minority women graft survival at 1, 3, and 5 years was 97.0%, 94.0%, and 91.6%, respectively. Except for 3-yr graft survival, graft and patient survivals at all three time points were significantly different (p<0.001) between minority and non-minority women. Multivariable analysis for graft loss[SO1] in women showed that age, creatinine, earlier transplant year, and immunosuppression all were significantly (p<0.04) associated with graft loss, but minority status was not.

Conclusions: Women with NASH cirrhosis have a higher MELD at LT than men. Minority women with NASH in particular have a higher MELD and Cr at time of transplantation compared to white women. Minority women are most vulnerable on the LT wait list. Even after LT, minority women exhibit worse outcomes compared to men or white women. Further work is necessary to elucidate these gender and racial difference after LT.
347.6

Racial-Ethnic and Sex Disparities in Access to Renal Transplant Waitlisting Vary by Age in the United States

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Background: Transplantation provides numerous benefits, but racial/ethnic and gender disparities in access to renal transplantation exist globally. However, in the United States, the interaction between race/ethnicity and gender in transplant access has not been well explored. Further, it is unclear how age at diagnosis modifies these disparities.

Methods: We used the United States Renal Data System to identify a retrospective cohort of incident adult dialysis patients from January 1, 2005 – December 31, 2017 and followed through 2018. We used multivariable Cox regression to model the association between combined race/ethnicity and sex (race x gender) group and time to renal transplant waitlisting. We adjusted for clinical and sociodemographic factors and included a time-dependent covariate reflecting a 2014 change in the national kidney allocation policy (KAS) aimed to improve equity. We incorporated a race x gender x age group interaction term to test for effect modification by age group. We also conducted stratified analyses per age group.

Results: After excluding prior renal transplant recipients (n=5,227) and preemptive transplants (n=3,486), we identified 1,337,386 US incident dialysis patients of whom 19.4% were waitlisted (median time to waitlisting (interquartile range): 350 days (184, 651)). Most patients were over 50; 50-59 (n=215,028, 19.8%), 60-69 (24.8%), or 70 or greater (37.2%). Waitlisting was highest among Asian women aged 18-39 (n=6,260, 69.7%) and lowest among Hispanic women aged 70 or greater (n=2,315, 1.9%). We found significant effect modification by age in the association of demographic group and time to waitlisting (p-value: <0.0001).

Across all age groups, Black women experienced reduced access to transplant waitlisting compared to age-matched white men; this disparity was worst among the oldest (aged 70 or greater) (adjusted hazard ratio (aHR): 0.60, 95% confidence interval (CI): 0.56, 0.64) and youngest (aged 18-39) Black women (aHR: 0.77, 95% CI: 0.74, 0.79). Furthermore, older Hispanic and white women (60-69 and 70 or greater) exhibited reduced transplant access compared to age-matched white and black men within their own race/ethnic group. Hispanic women aged 70 or greater experienced worst disparity with 42% reduced likelihood of waitlisting compared to white men (aHR: 0.58, 95% CI: 0.53, 0.64). Conclusions: The interaction between race/ethnicity and gender in access to renal transplant waitlisting in the United States varies significantly by age. Older Black and Hispanic women and younger Black women have significantly reduced access to transplantation compared to other groups, even after adjusting for clinical and sociodemographic factors. More work is needed to understand and ameliorate these interactions of gender, race/ethnicity, and age-related disparities to promote equity in access to renal transplantation.

This research was supported by University of Chicago Medicine’s Center for Healthcare Delivery Science and Innovation (HDSI), the Bucksbaum Institute for Clinical Excellence at the University of Chicago, and the National Kidney Foundation of Illinois. We also acknowledge the University of Chicago Research Computing Center for computational support of this work. The data reported here have been supplied by the United States Renal Data System (USRDS) and the United States Census Bureau. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the U.S. Government.
Impact of Gender on Kidney Transplantation Practices: A Single Centre Report From Largest Public-Sector Transplant Center of India

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Introduction: There is scarcity assessing the true burden of gender disparity in organ transplantation from the developing world.

Methods: We analysed data from 1997 to March 2020, comprised of a total of 5838 kidney transplants including 943 deceased donor kidney transplants (DDKTs) in addition to 4895 LDKTs including 440 living donor kidney paired donations. We excluded the data from pandemic period to avoid bias of low transplant volume in the period.

Results: A majority of male recipients have received DDKT. Interestingly, there have, however, also been more male deceased donors (Figure 2A, 2B). Of 831 DDKT recipients between 1997 and 2018 in our center, 68% have been males and 32% females. Overall, female donors constituted 71% of the living donor pool. Female donors are most frequently mothers (33.7%), wives (20.1%), and infrequently daughters (0.4%). When parents donate, it is most frequently the mother (73%). Donation rates of Fathers have increased from 10% in 1999 to 15% in 2020, reflecting a trend that focuses on the well-being of the nuclear family. For married couples, 90% of donors come from wives based on sociocultural reasons and a financial dependency on the husband. Figure 1 indicates that females (mother and wife) contribute to 50% of living donors. The contribution of Mothers increased from 20% in 1999 to 30% in 2020. Donations by other than near-related donors (near-related donors include parents, spouse, siblings, children, and grandparents) declined from 25% in 1999 to 3% in 2020 (Figure 1A, 1B). THOA has permitted kidney exchanges, also called swap transplants since 2011. From 2000 to 2020, 9.3% of all living donors have been through paired kidney exchanges. Female donors have contributed with (78%) to this program. Gender disparities become even more pronounced in pediatric kidney transplantation (Figure 3).

Conclusion: Gender disparity in transplantation our report is evident and can be combated by and the developing implementation of an equitable deceased donor allocation system, prioritizing difficult to match female recipients in a team effort with local living donor champions ensuring logistics and social support. The decision to donate among women is highly influenced by their roles within the family and society. Although the implementation of those policies is relevant, the hard work addressing social biases and financial disadvantages will need to happen in parallel.
Gender Disparity- A Battle Ongoing

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Introduction: Gender equity is a prominent issue in the medical profession. There has been a significant rise in the representation of women, but glaring discrepancies in the number who occupy lead roles as compared to men. Diversity enhances positive outcome for patients. We aim to assess the effect of gender equity initiatives

Method: Analysis of relevant literature from 2000-2020, depicting gender disparity in the medical profession was done and discrepancies in the number of women to men in the higher echelons noted as also the actions taken at various levels to promote equity

Results: A WHO analysis on gender equity demonstrated increasing women’s representation in health since 2000, an average gender pay gap of 28%. In India the pay gap is 34%. Female conference speakers spanning a decade significantly increased from Mean of 24.6% for 40 meetings in 2007 to 34.1% for 181 meetings in 2017. Women remain under-represented in academic surgery despite increasing percentages of female surgeons and residents, who have fewer total publications and are less likely to be listed as first author. Johns Hopkins University School of Medicine (JHUSOM) initiated Gender Equity Initiative with success. Salary gap decreased from -2.6% to -0.3%, but a lag existed in promotion despite a significant proportion at the lower faculty ranks. 5 articles published in JAMA Network Open (2018-19) showed that disparities not only limit women’s career trajectories but also have a significant impact on their compensation and retirement security. The Lancet group made a public commitment to promoting gender equity and increasing women representation. The Transplantation Society’s Women in Transplantation initiative has offered funding for research on sex and gender issues in solid organ transplantation and immunology. It has created the Woman Leader in Transplantation Award. Despite these endeavours, only 2 of 6 awardees of the Leslie Brent and Anthony P Monaco award for outstanding paper published in transplantation, 2 of 34 recipients of Medawar prize for outstanding contribution in the field of transplantation and 2 of 24 recipients of Thomas E. Starzl prize in Surgery and Immunology were women showing the gross neglect.

Conclusion: Gender transformative policies are needed to address inequities and eliminate gender-based discrimination in earnings and support access to professional development and leadership roles. Equal representation forms an essentiality rather than a vision.

Keywords: Gender disparity, women in transplant, Gender Equity Initiative.

Worse Graft Outcome After Pregnancy in Female Transplant Recipients

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Introduction: Fertility and sexual functions could rapidly restore after successful renal transplantation (RTx). This study was to examine the outcomes of pregnancy and graft survival between genders in our RTx recipients, and perinatal and fetal complications.

Methods: From May 1983 to December 2021, a total 1514 patients received RTx at our center, and 790 recipients within reproductive age (15-45 yrs, Female/Male: 344/446). There were 31 pregnancies recorded in 24 female recipients with 6 multigravida and one twin pregnancy, while 26 male recipients have their couples to get 35 pregnancies (including 8 multigravida).

Results: There was no difference between age of pregnancy, interval between RTx to delivery, immunosuppressive agents, and serum creatinine (sCr) before and after pregnancy. Female pregnancy recipients had more frequent in hypertension, urinary tract infection, anemia, and preeclampsia. The gestational age at delivery was 36.6 ± 3.6 weeks in female group significantly shorter than that of in male group (38.8 ± 0.7 weeks, P = 0.027). The birth weight/fetal length is 2470.7 ± 497.2 gm/45.9 ± 3.7 cm in female RTx recipients lower than 3172.7 ± 244.4 gm/48.8 ± 1.2 cm in male (P = 0.000). Unfortunately, the deterioration of graft function of sCr is from 1.8 ± 0.7 vs. 1.4 ± 0.4 mg/dL in year 2 to 2.0 ± 0.8 vs. 1.4 ± 0.4 mg/dL in year 3 between female vs. male RTx recipients. There are 10 graft failures in female group (66.7%), but none in male group during the follow-up period (P = 0.000).

Conclusion: In conclusion, our limited experience disclosed poor graft function and survival in our female recipient with pregnancy, and more low birth weight of fetus and preterm delivery. Female RTx recipients should be closely antenatal, perinatal and postpartum monitored to avoid complications in pregnancy.
Gender Equality in Heart Transplantation: A Single Centre Study

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Background: International Society for Heart and Lung Transplantation categorises female gender in donor/recipient, as a significant risk factor for mortality after heart transplantation. Further, donorrecipient gender mismatch is also reported to be a determinant of post-transplant morbidity/mortality. To examine the effect of gender in survival outcomes, we conducted a retrospective study.

Methods: Population comprised of 298 patients undergoing heart transplantation from 2001 to 2021, divided into four groups on the basis of donor and recipient matching. Group A consisted of men who received male donor-hearts, group B of women who received female donor-hearts, group C of women who received male donor-hearts, and group D of men who received female donor-hearts. Standard heart transplantation protocols were applied to all patient groups for graft preservation, surgical technique, donor-recipient size matching, induction&immunosuppressive-therapy.

Results: The study groups were found to be homogeneous to the major preoperative- risk- factors (aetiology, transplantation status, donor-recipient age, total ischemic time). Donor gender, recipient gender and donor-recipient gender mismatching did not significantly modify the short and mid-term survivals, functional recovery and primary graft dysfunction post-surgery.

Conclusions: Even though previous reports suggest that gender negatively affects survival, this proved to have no influence on the outcomes in our study. These results can be explained by a correct donor-recipient size matching. The well-documented female recipients’ tendency to more frequent and fatal rejection was not confirmed in our experience. The patient’s age at transplantation, the routine use of induction therapy and an aggressive immunosuppressive regimen may be the substrate of these findings. Student Finance England for supporting the study financially.

Transplant Pregnancy Registry International - 30 Years of Data Collection

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2021 marked 30 years of continuous data collection by the Transplant Pregnancy Registry International (TPRI). Since 1991, the TPRI has studied pregnancies in solid-organ transplant recipients. In 2016 the TPRI expanded to include international participants and pregnancies from 25 different countries are now included. Data are collected via telephone interviews, online questionnaires, and review of medical records. The TPRI follows participants and their children indefinitely. To date, 1,836 female solid organ transplant recipients, including 1,251 kidney recipients, participate in the TPRI (Table).

Table: TPRI: Pregnancy Outcomes in Female Transplant Recipients

<table>
<thead>
<tr>
<th>Organ</th>
<th>Recipients</th>
<th>Multiple Births</th>
<th>Total Births</th>
<th>Additional Conception Losses</th>
<th>Estimated Live Birth</th>
<th>Multiple Birth Losses*</th>
<th>Estimated Multiple Births</th>
<th>Mean Gestational Age/ Birthweight (weeks/ grams)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>1251</td>
<td>2233</td>
<td>85</td>
<td>2318</td>
<td>1967-2020</td>
<td>583</td>
<td>1735</td>
<td>35.8/ 2555</td>
</tr>
<tr>
<td>Liver</td>
<td>363</td>
<td>716</td>
<td>18</td>
<td>734</td>
<td>1985-2020</td>
<td>206</td>
<td>529</td>
<td>36.7/ 2772</td>
</tr>
<tr>
<td>Heart</td>
<td>110</td>
<td>187</td>
<td>5</td>
<td>192</td>
<td>1987-2020</td>
<td>62</td>
<td>131</td>
<td>36.2/ 2595</td>
</tr>
<tr>
<td>Kidney-Pancreas</td>
<td>71</td>
<td>131</td>
<td>8</td>
<td>139</td>
<td>1989-2019</td>
<td>45</td>
<td>94</td>
<td>34.1/ 2142</td>
</tr>
<tr>
<td>Lung</td>
<td>41</td>
<td>54</td>
<td>2</td>
<td>56</td>
<td>1992-2020</td>
<td>21</td>
<td>35</td>
<td>34.0/ 2192</td>
</tr>
</tbody>
</table>

Total/Overall 1,836 3,321 118 3,439 1967-2020 917 2,523

*includes: miscarriages, terminations, ectopic and stillbirth pregnancies
**348.1**

**Implementation of Quality Indicators for Organ Donation in Two Hospitals of Dominican Republic**

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**Introduction:** Worldwide, organ donation and transplantation has become a practice that can prolong and improve quality of life. While organ donation from deceased donors has increased exponentially over the years, the supply and availability of donors remain insufficient. (1) Implementation of safety and quality protocols within the health care organization is required to maintain public trust and effectiveness of organ donation and transplantation programs. (2) These guidelines aim to guarantee complete documentation and transparency throughout the process, from donation to transplant, enabling traceability and further assessment for continuous improvement of the system. (2) Moreover, to provide local, national, and regional data that allows to compare outcomes of the implementation of specific quality indicators, such as sociodemographic characteristics, health care structure, and economy.

**Method:** The study is multicenter, retrospective analysis of all deaths reported between January 2015 and December 2019 in the intensive care unit (ICU) of two trauma centers in Dominican Republic with Brain Death Donors (DBD) programs within their neurosurgery units and a transplant coordinator on-site. Indicators of the DOPKI study (3) were used to measure the donation potential, the effectiveness of the donation process, and the points to improve in the organ donation process for public policies to be instated.

**Results:** From all deaths reported in ICU between 2016-2019, the median potentiality for DBD was 27.5% and 6.2% in hospital A and B, respectively. Conversion rate of all the brain deaths to real donors was 6.2% and 5.9%, being 2019 the year with the highest conversion rate. Major causes of donor loss were family refusal (26.5% and 14.8%) and donor maintenance failure with (21.2% and 23.5%).

**Conclusion:** While both hospitals shared the highest rate of devasting cerebral lesions cases in the country and manage similar number of neurotrauma in their ICUs, hospital A showed better indicators for donor potentiality when compared to hospital B. These findings might be attributed to the lack of a 24/7 donation team to help detect in time potential organ donors and the need to implement an alert system to notify the donation team when these cases occur. The low conversion rates on both hospitals are due importantly to high rates of family refusals and donor maintenance failure and should be areas of improvement. National media campaigns raising awareness and emphasizing values of altruism and solidarity improve the perception of families and society about organ donation and decrease the family refusals. The development of a Donor Management Protocol must be carried out and established, to be implemented in hospitals with donor-generating capacity created by a multidisciplinary team lead by of the National Government Transplant Office and socialized with all the key professionals involved in organ donation and transplantation to minimize the maintenance failure.

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**348.2**

**Beyond Black and White: A National Study of Asian Americans’ Willingness Toward Organ Donation**

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**Background:** Asian Americans (AA) are the fastest growing racial group in the US, but health disparities research has focused primarily on Black and Latinx Americans. Transplantation research is no exception. Asian Americans’ needs for transplantable organs are substantial, but they have the lowest rates of organ donation per million compared to other Americans by race. Over the past 20 years, the literature about AA attitudes, beliefs and behaviors around organ donation is limited. To better understand AAs’ disposition towards organ donation, a national self-administered survey was developed and disseminated.

**Methods:** The final national survey was the result of formative research and community-engaged efforts to ensure that study implementation was culturally appropriate and targeted to AAs. To inform survey development, focus group interviews were conducted with AA participants representing multiple ethnic and age groups, immigration experiences, and education levels. The final survey instrument was deployed online, and quota sampling based on the 2017 American Community Survey of the US Census Bureau was used to achieve a sample representative of the US Asian population. Bivariate tests using logistic regression and the chi-square test of independence were performed.

**Results:** Recruitment yielded a final representative sample of 899 respondents. Over half (58.1%) were willing to be organ donors. Willingness to donate one’s own organs was not associated with ethnicity, but statistically significant associations were found with respondents’ age, education, income, nativity, and religion. A majority (81.8%) expressed a willingness to donate a member’s organs, but the degree of enthusiasm depended on the family member’s known donor wishes. Nativity, higher education, and religion were significantly associated with the willingness to donate a family member’s organs. Only 9.5% of respondents indicated that the decision to donate their organs was theirs alone to make; the remainder would involve at least one other family member.

**Conclusion:** To the authors’ knowledge, this is the largest study on Asian Americans’ Willingness Toward Organ Donation. Recruitment yielded a final representative sample of 899 respondents. Over half (58.1%) were willing to be organ donors. Willingness to donate one’s own organs was not associated with ethnicity, but statistically significant associations were found with respondents’ age, education, income, nativity, and religion. A majority (81.8%) expressed a willingness to donate a family member’s organs, but the degree of enthusiasm depended on the family member’s known donor wishes. Nativity, higher education, and religion were significantly associated with the willingness to donate a family member’s organs. Only 9.5% of respondents indicated that the decision to donate their organs was theirs alone to make; the remainder would involve at least one other family member.
Prevalence of Chagas Disease in Deceased Donors From Argentina

Ariel Antik1, Gabriela Hidalgo1, Margarita Anders4, Federico Piñero3, Daniela Hansen Krogh1, Viviana Tagliafichi2, Marcelo Silva2, Manuel Mendizabal3, Florencia Antinucci4, Julia Bruttì5, Liliana Bisigniano2.

Background & Aims: Argentina is an endemic area of Chagas disease, estimating that there are around 2 million infected. However, the real prevalence of the disease is unknown. Thus, the aim of this study is to evaluate the prevalence and utilization of donors with Chagas disease in Argentina.

Methods: We performed a cross-sectional study to analyze data from the National Procurement of Transplantation (INCUCAI) in Argentina from 2006 to 2020. We included data from all donors, including effective organ donors (those for whom transplantation was effectively done), non-effective organ donors, and tissue only donors that were discarded. Chagas serologic tests included Immunoglobulin, enzyme-linked immunosorbent assays and complement fixation. These tests were performed in all donors during the procurement process. A donor was considered positive when at least two of the three tests turned positive. A stratified analysis according to the type of donor and Chagas status was done.

Results: Overall, 16140 deceased donors were included. Organ donors 8627 (55%), and 7513 (46%) tissue donors. Demographic characteristics age 42 ± 18 years and male/female ratio was 1.59/1. Overall serologic tests showed that the prevalence of Chagas disease in deceased donors was 3.27% (n=528). The highest prevalence was found in the provinces of Chaco (11.7%), Santiago del Estero (10.7%) and Formosa (8.6%). Prevalence ratio per periods among Chagas + donors showed that the highest prevalence was observed in 2010 (6%) and the lowest prevalence in 2020 (1.8%). The percentage of effective donors among those with positive Chagas was 85%, lower than the effective donors chagas negative which is 90% (p=0.001). The solid organ transplants performed using chagas positive donors were 234 kidneys and 87 livers.

Conclusions: The prevalence of Chagas in deceased donor in Argentina is high, especially in the northeast region. Since the probability of being a donor is random, the prevalence in this population could be close to the real one in the country. A lower percentage of effective organ donors chagas positive is observed, so these type of organ donors could be optimized.

An Analysis of Institutional Communication Strategy To the Increased Social Media Demands in Transplantation in Argentina

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Introduction: For more than a decade, the Central National Institute for Ablation and Implant (INCUCAI, Argentina) has been using social networks to communicate with the community. The availability of affordable communication devices such as smartphones connected to the internet favored the use of social networks. Regarding donation and transplantation, social networks are used to share information but also to consult issues related to the demands of transplant recipients, people on the waiting list and their relatives, family members of donors and members of the community to connect with each other, collect news and information, but also create and share content. Among the social networks used by the INCUCAI, Instagram is the one that has experienced the greatest growth in recent years. The aim of this study was to analyze the inquiries and comments of Instagram users to our Institution and the performance of our Institution in meeting the demands of social network users.

Methods: We carried out a quantitative and qualitative analysis of the comments made by Instagram users to our publications, as well as the private messages sent and the responses made by our institution between January 1st and December 31st, 2021. The analyzed parameters included the total number of comments; the comments that required some type of official response from our Institution; the type of inquiries, i.e., requests for information or complaints.

Results: During the year 2021, a total of 3,877 comments (in publications and private messages) were registered on the INCUCAI institutional Instagram network. Of the total comments, 871 (22%) required some type of institutional response. The qualitative analysis of the comments that required an institutional response showed that 679 comments (78%) requested information, while the remaining 192 (22%) corresponded to complaints. The analysis of the requested information was as follows: 423 (48.5%) were queries from patients in the transplant registration process, on the transplant waiting list, as well as transplant patients or their relatives; 163 (18.7%) were inquiries about organ and tissue donation and information about the donor registration process; 267 (30.6%) were queries about hematopoietic stem cell transplantation and queries about the registration process in the bone marrow registry; 18 (2%) corresponded to contacts made by relatives of donors. It is important to mention that of the total number of comments that required an institutional response, 687 (81.9%) were answered in less than 48 hours.

Conclusion: The analysis of the data confirms that a significant number of people use social networks to demand an institutional response. Most of the consultations correspond to the needs of the patients (transplanted and on the waiting list). Proper use of social networks by institutions linked to the donation and transplantation process probably requires quick responses to queries, this being a priority for INCUCAI.
Life Threatening, Cytokine Release Storm (CRS) With Anti Thymocyte Globulin (ATG) And Its Management

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Introduction: Cytokine Release Storm (CRS) leading to fatal or near fatal hypotension has been reported in association with anti thymocyte globulin (ATG) administration. This is a very rare and unusual manifestation of ATG and early recognition and management of this unexpected manifestation will help save lives. We report a near fatal case of CRS, during renal transplantation, associated with ATG administration, its diagnosis and management.

Materials and Methods: A 27-year-old, otherwise healthy male with Alport’s syndrome was undergoing live related preemptive renal transplant. Patient received morning dose of Solu-Medrol and CellCept and was getting Anti Thymocyte Globulin (ATG) slowly after the test does, as the recipient vascular bed was being prepared. Patient started to become hypotensive which was treated with IV fluids and pressors including norepinephrine, epinephrine and dopamine. There was no bleeding from recipient vascular bed. A stat chest x-ray, EKG and echocardiogram on the OR table were normal with good LV function. Despite maximum dose pressor support and IV fluids, the mean blood pressure was around 45 - 50 mm Hg and a systolic blood pressure was around 65-70 mm Hg, leading to severe metabolic acidosis and lactate buildup. The transplant was canceled and the donor was closed unharmed and the patient was moved to ICU, intubated. His response to colloids was slightly better, but transient, so he was transfused 4 units of blood as volume expander that does not leak into 3rd space. This brought his blood pressure to about 90 mm Hg. A presumptive diagnosis of ATG induced CRS was made. His inflammatory markers including IL-6, ferritin, D-dimers and CRP were very high. 400 mg of Tocilizumab (Actemra) an IL-6 inhibitor along with broad-spectrum antibiotics were given. Patient also started to developed disseminated intravascular coagulation (DIC) with deranged coagulation screen and some oozing from the wound which was treated with FFPs. In next 12 hours, the patient started to stabilize and in next 48 hours he was extubated.

Discussion: Cytokine Release Storm (CRS) is a potentially fatal condition unless recognized and treated early and aggressively. In COVID pandemic, much better understanding of CRS along with its symptomatology, easy availability of its lab tests and IL-6 inhibitors became possible. High index of suspicion is extremely important in making an early diagnosis and for early treatment. In transplant patients, use of ATG is now standard of care and very few cases of ATG induced CRS are reported. In our case, early diagnosis of CRS from ATG, use of blood as volume expander, early administration of IL-6 inhibitor and aggressive management of DIC turned out to be the life Saver.

Conclusion: In patients receiving ATG, with unexplained hypotension, non-responsive to IV fluids and pressors, high index of suspicion of ATG induced CRS with early diagnosis and aggressive management can save lives.
Renal Transplantation Experience in the Last 5 Years in the Adult Intensive Care Department of the Hospital de Clínicas

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Introduction: In December 1985, the first renal transplant was performed at the Hospital de Clínicas. This multidisciplinary team continued to work in a coordinated manner to respond to the increasing needs of patients requiring this therapy. The objective of this paper is to expose the experience in renal transplants of the Adult Intensive Care Department of the Hospital de Clínicas of the Facultad de Ciencias Médicas from the Universidad Nacional de Asunción in the last 5 years.

Methodology: An observational, descriptive, retrospective, and cross-sectional study was conducted. Medical records of all patients admitted to Adult Intensive Care in the postoperative period of renal transplantation from January 2017 to December 2021 were used.

Results: During the study period, 54 patients were submitted to renal transplantation, 72.2% of whom were male (n=39). The median age was 34 years old (IQR:21). Co-morbidities were arterial hypertension 85.1% (n=46), hypothyroidism 9.2% (n=5), polycystic kidney disease 9.2% (n=5), diabetes mellitus 7.4% (n=4), glomerulonephritis 5.5% (n=3) and rheumatologic diseases 5.5% (n=3). The prognostic score used was APACHE II, with a median of 11 (IQR: 3). The median number of inpatient days was 3 (IQR: 2). Mechanical ventilation was required in 7.4% of patients (n=4) and the average number of ventilator days was 9 (range: 2-19). Continuous furosemide infusion was required in 50% of patients (n=27). Patients received vasopressors in 12.9% (n=7). Of the patients studied, 96.2% were on hemodialysis (n=52). The median age of patients who required hemodialysis was 4.9 mg/dl (IQR: 5.1). The transplanted kidney came from a living donor in 38.9% (n=21) and from a cadaveric donor in 61.1% (n=33). Eight patients required post-transplant hemodialysis sessions, seven of them from cadaveric donors. Doppler ultrasound of the transplanted kidney showed renal artery stenosis in 12.9% (n=7), with clinical repercussions in 2 patients, leading to transplantectomy in one of them. Survival to discharge from the intensive care unit was 100%.

Conclusion: Renal transplantation, both from living and cadaveric donors, is a valid therapeutic option with good results and low complications for patients with end-stage renal disease.

Evolution of Brain Deaths in the Argentine in 2019-2021

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Introduction: Declaration of brain death (BD) and subsequent management of potential donors for organ transplant along with obtaining the consent of the family for procurement is a highly sensitive issue. The Argentine Law 27447, approved on 2018, makes all citizens donors unless they explicitly express otherwise. Thus, in 2019 transplants increased almost by 60% compared to 2018. In the present work, and in order to deeply analyze the evolution of the brain donors, we studied the management of brain death patients as transplant donors.

Methods: The National Transplant Information System (SINTRA) was used to analyze the evolution of the total number (3038) of certified brain deaths in the Argentine Republic during the 2019-2021 period. Ages between 1 day and 83 years. Average age: 41.1 years. 39% female and 61% male. The analysis included 437 public and private institutions of the 24 jurisdictions of the Country.

Results: From a total of 3038 certified BD, 83% (n = 2535) was approached to family for the donation. Only 7% (n = 138) of them presented express manifestation in life about donation (15% negative, and 85% affirmative), while 82% (n=2075) and 11% (n=335) were done to relatives of potential adult and 18 younger age donors, respectively. It is important to mention that, according to law 27447, potential adult donors are considered presumed donors. Among adult donors, 91% were affirmative and 9% negative, while for donors under 18 years of age were 43% negative and 57% affirmative. Among the total number of BD, 64% (n=1967) became real donors. The remaining 36% were not ablated due to: opposition to donation (11%, n = 335), cardiac arrest prior to ablation (3%, n=101), judicial refusal (0.75%, n=23), other causes of non-ablation (1%, n=33), and absolute medical contraindication (19%, n=589), of which 7% (n=39) (7%) were ruled out due to COVID-19 (29 in 2020 and 10 in 2021).

Conclusions: The lowest rate of opposition to donation was observed in the group of potential donors considered presumptive donors. This allows us to conclude that Law 27447 is an effective tool when communicating the donation, exempting family members from having to make the decision. The highest rate of opposition to donation was observed in the group of minors, in whom the family is the one who must decide on the donation. Likewise, regarding the manifestations of donation by the family, it was evidenced that the majority of the people made an affirmative organ donation. Overall, most of the BD detected became real donors, being those that did not, due to unexpected/reasonable causes, and even with percentages below those considered at the international level, demonstrating the optimization and quality of the process from its beginning.

Acknowledgement to Dr. Carlos Soratti for his support and stimulation for work.
Impact of COVID-19 on Organ Procurement in Argentine

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Introduction: There is no doubt that SARS-CoV-2 pandemic has had a negative impact on worldwide health care system. Several factors might have been affected the process of organ donation and recovery, such as adequate donor evaluation and consent, hospital resources among others. The aim of the present study was to analyze and compare the quality metrics in organ donation before and during SARS-CoV-2 pandemic.

Methods: A retrospective, descriptive study was conducted with data obtained from the Reporting Center of the Argentine National Transplant Information System (CRESI) before (2019) and during pandemic (2020 and 2021). Data collected included: brain deaths detected, real deceased donors, effective donors (donor from whom a perfused organ was removed and implanted in a recipient), multi-organ donors, opposition to the donation, total number communications for donation, and solid organ transplants performed with cadaveric donor. The quality indicators used were: Donors per million inhabitants (DPMH); Conversion rate (CR = real donors/detected brain deaths); Effectiveness (Ef = Real donors/effective donors); multi-organ donor rate (MODR = multi-organ donors/ actual donors); Opposition rate (OR = opposition to the donation/total communications made); solid organs procured by real donor (SOPRD = organs/ real donors), and solid organ transplants performed with cadaveric donor (SOT = solid organ transplants/ real donors).

Results: Table 1. The DPMH rate decreased by 50% in the first year of the pandemic, partially recovering in the second year with a 30% decrease compared to 2019, probably due to the epidemiological context and the logistical barriers. However, during 2021, the CR gradually increased likely due to the development of efficient protocols, a decrease in the number of COVID-19 cases, and the reorganization of human and technological resources, and improvements of the intensive care units. Surprisingly, the percentage of Ef of the donation process increased in both years of the pandemic, as did the MODR. Regarding the OR, there was an increase in the first year of the pandemic but a decrease of 2 points in the second year of pandemic. Even though, all years analyzed the OR was below the desired 20 % value. Likewise, the SOPD and SOT slightly increased in pandemic compare to 2019.

Conclusions: Although the absolute numbers showed a significant decrease in organ donation during pandemic, the quality indicators of the donation process were maintained and even improved for the same period, probably due to the strategies executed with the aim to mitigate the impact of the pandemic due to SARS-CoV-2 over the donation, procurement and transplantation process.

Acknowledgement to Dr. Carlos Soratti for his support and stimulation to work.
The “Global Kidney Exchange” Proposal Is Impractical And Not Financially Neutral

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This paper argues that, notwithstanding some recent claims by moral philosophers, the proposed Global Kidney Exchange (GKE) should be rejected as impractical and not fair. The key problem with the GKE is that it would allow intergovernmental bodies (such as the World Health Organization) and professional societies (such as The Transplantation Society and the Declaration of Istanbul), and would violate national laws that forbid organ trafficking and that require financial neutrality in organ donation. Under the proposal, a kidney patient in a high-income country (HIC) who is biologically incompatible with his or her donor would be matched with a prospective donor from a low/medium-income country (LMIC) who is willing to donate to a patient there who cannot get a transplant for lack of the necessary funding or facilities. The GKE would bring the LMIC pair to the HIC, coordinate the two transplant operations (LMIC donor to HIC recipient and vice versa), and fund a US$50,000 escrow account for follow-up care of the LMIC pair, including the recipient’s post-transplant immunosuppression.

A normal “kidney swap” meets ethical and legal requirements because only organs are exchanged, whereas in the GKE an LMIC patient who can supply a donor who meets the GKE’s requirements will receive not only a kidney but substantial financial benefits. Since the exchange is not financially neutral, the Council of Europe has rejected the GKE as a form of “organ trafficking” and an exploitation of financial inequality. In response, recent defenders of the GKE have made several arguments. First among these is the claim that saving recipients’ lives outweighs all the objections raised to the GKE; the preferences of the LMIC donor, who might prefer something else to saving the recipient, are ignored.

Besides being unethical, the proposal is impractical. Some patients from LMICs will respond to the possibility of an organ transplant by recruiting paid donors and disguising them as an altruistic friend or relative, a ruse that is contradicted by experience: donation rates are much higher in countries such as Spain and the US than in countries where payments occur such as Iran and Saudi Arabia. Furthermore, the proposal is impractical because the GKE does not provide, as the philosophers claim, “an eminently fair solution” to the inequities that face LMICs. Besides being unethical, the proposal is impractical. Some patients from LMICs will respond to the possibility of an organ transplant by recruiting paid donors and disguising them as an altruistic friend or relative, a ruse that is contradicted by experience: donation rates are much higher in countries such as Spain and the US than in countries where payments occur such as Iran and Saudi Arabia.

Kidney transplant “vouchers” were created in 2014 as a means to overcome the “chronological incompatibility” that arises when a potential donor wants or needs to donate before the relative or friend who is to receive the kidney is ready to have a transplant. In exchange for the donor giving a kidney now, the prospective recipient is provided with what the National Kidney Registry (NKR) calls a “Standard Voucher” (SV), which can be redeemed when the recipient is ready for a transplant. In this paper, we describe the benefits of extending this innovation to altruistic donation and examine preliminary data on the effects.

The kidneys supplied by altruistic donors are critical to the success of transplant chains because they typically serve as a non-directed donation that sets in motion a chain of many biologically incompatible donor-recipient pairs. Well-designed chains make possible a large number of transplants which would otherwise not have occurred or would have taken much longer to arrange, especially for highly sensitized or O blood-type recipients. The innovation—termed “Family Vouchers” (FVs) by the NKR—overcomes the “sentimental incompatibility” that leads some potential altruistic donors to back away from donating when they realize that giving a kidney to a stranger now will preclude them from providing a kidney should a loved one need a transplant in the future. FVs differ from SVs because donors are permitted to list up to five intended recipients, though only one may redeem the FV, and the intended recipients do not then have terminal kidney disease and may not develop it in the future. Like SVs, FV-based donors initiate kidney chains, which end with a recipient who lacks a donor. Likewise, the transplant network that issues the voucher will provide a suitable kidney at the end of a future chain when the designated recipient redeems the voucher.

The expectation that FVs will attract new donors as well as provide assurance to people who develop doubts about their plan to make an altruistic donation is supported by current data. For example, voucher-based donation, which accounted for a tiny fraction of nondirected donation in the US when it began in 2014 had surpassed altruistic donation by 2019, and its rapid growth helped nondirected donation to triple by 2021 (Figure 1). The Covid-19 pandemic interrupted this steady rise, but the decrease in nondirected donation was much smaller than for living kidney donation generally (Table 1). While altruistic donation went down, the rise in FV-based donations meant that in 2021 the percentage of living donors who were nondirected was the highest ever. Family Voucher programs, which are aligned with a central goal of transplant professionals—shortening the wait for transplants—need to broaden their outreach in minority communities and to carefully self-monitor their ability always to fulfill their moral commitment to provide all voucher-holders with a kidney from a suitable living donor.

Figure 1: Number of patients participating in standard altruistic and FV based donation from 2014 to present (A). Percentage of non-directed donation by either standard altruistic or FV based donation (B). Numbers reflect to June 2021.
400.3

One Organ Procurement Organization's Effective Strategy For Dramatically Increasing Donation After Circulator Death Donation and Transplantation

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Introduction: Donation after circulatory death (DCD) represents a viable organ donation option in scenarios where a patient doesn’t meet strict brain death criteria. DCD has been proven to increase the supply of donor organs for transplantation. DCD has been a standard of practice for over two decades in this Organ Procurement Organization, ensuring that every opportunity to honor a patient's decision or to offer donation to a family was fully explored.

Methods: In 2021, the United Network for Organ Sharing (UNOS) led a ‘DCD Collaborative’. This OPO was one of 36 participants. The goal was to increase DCD 20%. To achieve the goal this OPO created and implemented an improvement strategy: 1. Establishing OPO metrics and key performance indicators; 2. Implementing an Improvement Team (seven Transplant Surgeons, seven Critical Care Physicians) responsible for driving results; 3. Formation of distinct ‘work groups’ to implement specific tactics (DCD physician survey, DCD resource guide, normothermic regional perfusion model, uncontrolled DCD hospital protocol); 4. Internal OPO strategy and collaboration within Transplant Coordinator and Hospital Development departments.

Results: Engagement was maintained through ‘DCD Improvement Team Meetings’ where a standardized agenda was utilized. Daily surveillance by Administrators on Call (AOC) guided clinical practice to rule-in every possible potential DCD candidate. A retrospective quality process was implemented to review rationale for ruling out patients as DCD candidates. Sharing of this information occurred at weekly AOC meetings. Customized data analytics were used to monitor outcomes and progress.

This OPO achieved a 48% increase in DCD donation and a 39% increase in DCD transplants. As a result of Hospital Development messaging for clinical referral triggers and aggressive clinical practice, the pool of potential DCD donors increased by 43%. Additionally, the focused education on preserving the donation opportunity resulted in an increase in the percentage of DCD cases that were facilitated in a controlled fashion. The OPO surpassed its goal of coordinating 30 DCD liver transplants. Authorization rates for DCD improved from 47% in 2020 to 51% in 2021. Twelve Improvement Team meetings and two physician-led DCD webinars occurred. Normothermic regional perfusion model protocol was adopted. A DCD physician survey was completed. Feedback is being incorporated into a DCD Resource Guide developed by the critical care physician work group.

Conclusion: Establishing clear goals, a comprehensive strategy and tactics created an environment that fostered focused attention on every referral of a potential DCD candidate. Incorporating active and retrospective quality components allowed OPO staff to be agile, adjusting clinical decisions quickly. Communication across OPO departments promoted idea sharing leading to robust team meetings and educational programming. Processes established during this initiative have been adopted as standards of practices.
Deceased Kidney Donor Acceptance Criteria: A Survey of Canadian Transplant Nephrologists, Surgeons and Urologists

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Introduction: Kidney transplantation provides a quality of life and survival advantage for patients with end-stage kidney disease (ESKD) relative to remaining on dialysis. However, the number of patients on the transplant waitlist is steadily increasing relative to the number of available kidney donors. Despite this, while Canadian organ discard rates are not available, the proportion of discarded kidneys in the United States has paradoxically increased over time. While there is an abundance of literature regarding predictors of organ decline in the United States, to date, there are no data regarding the rate or rationale for deceased donor decline in Canada.

Methods: We performed an online survey (July 22-Oct 4, 2021) to assess deceased donor acceptance practices of Canadian transplant nephrologists, surgeons and urologists. Surveys were distributed by email to members of the Canadian Transplant Society. Surveys consisted of 3 sections of increasing donor complexity and respondents were asked whether they would accept or decline a hypothetical donor presented in the question stem, assuming there was a suitable recipient. The proportion of respondents completing the survey was determined, as were overall and donor scenario-specific acceptance rates amongst those providing responses.

Results: A total of 81 respondents accessed the survey from 19 centers and seven provinces across Canada (all provinces with at least one transplant center). A total of 72 respondents (88.9%) answered at least one question and 16 respondents (22.2%) did not complete the survey. Donor acceptance rates for Sections 1 and 2 are demonstrated in Figure 2. Overall acceptance rates were highest for the younger (40 years) donor scenarios and when the donor was NDD vs. DCD. The most pronounced drop in acceptance rates for all donor scenarios was between a non-dialysis dependent donor with recovering AKI (92% acceptance) and a donor with AKI requiring dialysis and a biopsy demonstrating ATN but no coagulative necrosis (20% acceptance). Acceptance rates for Section 3 are demonstrated in Figure 3. The most pronounced drop in acceptance rates for all donor scenarios was between a deceased donor with comorbidities but no CKD (85% acceptance) and a donor with CKD and a biopsy demonstrating 3 out of 12 glomeruli sclerosed, but no arterial hyalinosis (25% acceptance). Overall, advanced donor age, DCD donor status, AKI, CKD and comorbidity burden were all associated with an increased risk of deceased donor non-acceptance.

Conclusions: Given relatively high rates of donor decline and apparent heterogeneity in acceptance decisions, Canadian transplant specialists may benefit from additional education regarding the benefits achieved from even medically complex or “marginal” kidney donors for appropriate candidates relative to remaining on dialysis on the transplant waitlist.

3 Sections with 8-16 cases each:

<table>
<thead>
<tr>
<th>Section</th>
<th>Donor Age</th>
<th>Donor Gender</th>
<th>Subsections</th>
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</thead>
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<td>1</td>
<td>NDD</td>
<td>Male</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>NDD</td>
<td>Male</td>
<td>3, 4</td>
</tr>
<tr>
<td>3</td>
<td>DCD</td>
<td>Female</td>
<td>1, 2, 3</td>
</tr>
</tbody>
</table>

Question Flow

- Step 1: Confirm donor age and gender
  - If donor age is NDD, proceed to Step 2.
  - If donor age is DCD, proceed to Step 3.

- Step 2: Assess donor gender
  - If donor gender is male, proceed to Step 3.1.
  - If donor gender is female, proceed to Step 3.2.

- Step 3: Evaluate donor complications
  - If donor has no complications, proceed to Step 3.3.
  - If donor has complications, proceed to Step 3.4.

- Step 3.1: If donor is male, assess specific complications
  - If donor has no specific complications, accept donor.
  - If donor has specific complications, reject donor.

- Step 3.2: If donor is female, assess specific complications
  - If donor has no specific complications, accept donor.
  - If donor has specific complications, reject donor.

- Step 3.3: If donor has no complications, assess organ quality
  - If organ quality is acceptable, accept donor.
  - If organ quality is unacceptable, reject donor.

- Step 3.4: If donor has complications, assess organ quality
  - If organ quality is acceptable, accept donor.
  - If organ quality is unacceptable, reject donor.

Begin subsection

- Profile 1: NDD male
  - Accept donor

- Profile 2: NDD male
  - Accept donor

- Profile 3: DCD male
  - Accept donor

- Profile 4: DCD male
  - Accept donor
Abstracts

400.5 Outcomes After Declining a Donation After Cardiac Death (DCD) Liver for Transplant Candidates in the United States

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Introduction: In the context of the deceased-donor liver shortage, donation after cardiac death (DCD) provides an opportunity to expand the donor pool, but DCD organs confer higher risk of biliary complications and graft loss. Patients and clinicians who are offered a DCD liver must choose whether to accept the higher risk or remain on the waitlist in hopes of a better offer. We explored outcomes of candidates who declined a DCD offer, and investigated the survival benefit accepting vs declining the offer of a DCD liver. In addition, we estimated the number of additional liver transplants that could be achieved if DCD livers were utilized at the same rate as livers from otherwise-comparable DBD donors.

Methods: Using national registry data from the United States (SRTR) 2009-2020, we identified 1,564 candidates who accepted DCD offers (“acceptors”) and 16,981 candidates who declined the same DCD offers (“decliners”). We characterized outcomes of decliners using a competing risk framework. In addition, we compared patient survival of acceptors vs. decliners using Cox regression. We used Poisson regression to compare observed discard of DCD livers to the number of discards expected based on donor characteristics other than DCD.

Results: Among DCD decliners, 50.9% died/dropped out from waitlist; only 43.1% were transplanted with a donation after brain death (DBD) liver. DCD acceptors had lower mortality compared to decliners at 10 years post-offer (35.4% vs. 48.9%, p<0.001) (Figure 1). After adjustment, DCD acceptors had 46% lower mortality risk compared to DCD decliners (aHR= 0.49 0.54 0.61). The survival benefit of DCD LT varied by MELD stratum. DCD offer acceptors had 55%, 34% and 52% lower risk of mortality compared to DCD offer decliners within MELD strata 15-24 (aHR= 0.39 0.45 0.54, p<0.001), 25-34 (aHR= 0.55 0.66 0.79, p<0.001) and 35 or higher (aHR= 0.29 0.48 0.78, p=0.004), respectively (Figure 2). Out of 1005 recovered DCD livers, 298 were discarded in 2019. If DCD livers were utilized at the same rate as comparable DBD livers, we estimated that 235 (78.9%) of them would have been transplanted.

Conclusions: Despite risk of biliary complications, DCD offer acceptance is associated with considerable long-term survival benefit for liver transplant candidates. Increased utilization of DCD livers should be encouraged.

This work was supported by grant number K01DK101677 (Massie), 5T32DK007713-23 (Eagleson), and K24DK101828 (Segev) from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The analyses described here are the responsibility of the authors alone and do not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products or organizations imply endorsement by the U.S. Government. The data reported here have been supplied by the Hennepin Healthcare Research Institute (HHRI) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government.
OPTN Kidney Allocation Policy Change Impact on OPO Resource Allocation

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Objective: This study evaluates the impact of the UNOS kidney allocation policy change requiring offers be made first to candidates at transplant hospitals within a 250-mile nautical radius of the donor hospital based on median allocation time expended by one large OPO with 78 transplant centers (including 14 local centers) that span 5 UNOS regions and 15 DSAs within its primary sharing radius.

Methods: This was a single OPO, multi-center observational study. Renal distribution time (RDT) defined as the time from donor cross-clamp to when a kidney is available to a center for a specific recipient including complete donor information and a compatible final cross match was evaluated for kidneys allocated 12 months pre and post policy change. Median RDT and utilization rates were evaluated for kidneys with KDPI < 60% and kidneys with KDPI >= 60%. The OPO continued hardwired best practices pre-recovery post policy change that included transplant center review of the offer, confirming patient(s) readiness and a final cross match for at least 5 candidates prior to recovery. The OPO also required an understanding with the accepting center at final kidney acceptance including confirmation of patient status, intent for pulsatile preservation, identified center back up patients and timing of transplant surgery.

Results: Between 3/15/2020 and 3/14/2021 pre policy change, the OPO recovered 1171 kidneys with a 73% utilization rate resulting in the transplantation of 859 kidneys. Between 3/15/2021 and 3/14/2022 post policy change, the OPO recovered 1336 kidneys with a 75% utilization rate resulting in the transplantation of 1005 kidneys. The proportion of kidneys placed locally decreased from 60% to 23% $X^2 (1, N = 1864) = 253.0262, p < 0.01$. Median RDT for kidneys with KDPI >= 60% increased significantly from 6.4 hours to 9.5 hours.

Conclusions: OPOs face increased challenges executing efficient kidney allocation, interacting with more centers per donor. Increased RDTs can be attributed to the number of transplant centers and patients within 250 nautical miles, increased interactions between OPOs and transplant centers, and transplant center use of third-party services that insulate the surgeon or nephrologist.

<table>
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<th>KDI</th>
<th>Pre Kidney Allocation Policy Change 3/15/2020 - 3/14/2021</th>
<th>Median RDT (hrs)</th>
<th>Utilization Rate</th>
<th>Post Kidney Allocation Policy Change 3/15/2021 - 3/14/2022</th>
<th>Median RDT (hrs)</th>
<th>Utilization Rate</th>
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<tr>
<td>EOR &lt; 60%</td>
<td>90% (105/115)</td>
<td>4.3 (2.5-13.1)</td>
<td>0.82 (0.62/0.87)</td>
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<td>EOR &gt;= 60%</td>
<td>75% (130/173)</td>
<td>4.3 (1.5-13.1)</td>
<td>0.85 (0.80/0.89)</td>
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<td>All KDI</td>
<td>75% (89/119)</td>
<td>5.4 (2.4-13.3)</td>
<td>0.87 (0.75/0.90)</td>
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<td>0.85 (0.80/0.90)</td>
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A Decade of Growth: One OPO's Journey to Excellence

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Background: In February 2012, one U.S. organ procurement organization (OPO) welcomed a new Chief Executive Officer (CEO). With Board support, the CEO initiated a new strategic plan focused on maximizing organ donation and subsequent transplant of donated organs through interventions including specialty requestors, in-house OPO coordinators, commitment to donation after circulatory death (DCD), and perfusion technology. We sought to quantify and categorize the growth experienced by the OPO in the ensuing decade.

Method: Twenty years of data (2002-2021) were analyzed, with comparison of the decade before the OPO’s new strategic focus compared to the decade since. Numbers and types of organ donors and organs transplanted from those donors were analyzed utilizing the OPO data warehouse and analytical software. Data were analyzed both by decade and by five-year cohorts.

Results: Between 2002 and 2011, the OPO recovered 2,527 organs that were transplanted from 851 deceased donors. Of these 851 donors, 28 (3.3%) were DCD and 828 (96.7%) were donation after brain death (DBD). From 2012 through 2021, 4,724 organs were transplanted from 1,693 donors, increases of 86.9% and 98.9% respectively. DCD increased to 569 (33.6%) of donors, with 953 organs transplanted from DCD (20.2% of total). Comparatively, total U.S. donors with the OPO removed increased by 36.1% when these two decades are compared.[1]

When subdivided into four five-year cohorts (A=2002-6, B=2007-11, C=2012-16, D=2017-21), the OPO’s results were as follows: donors recovered grew most dramatically between cohorts B and C, with increases for DBD (21.5%), DCD (554%), and total deceased donors (49.7%). Growth was sustained with increases from cohort C to D for DBD (15.7%), DCD (162%), and total donors (49.7%) (Figure 1). Comparatively, total U.S. donors less the OPO’s increased by 9.2% between cohorts B and C.[1]

Similarly, organs transplanted increased between cohorts B and C for DBD (41.4%), DCD (449%), and all deceased donors (56.2%). Growth was sustained with increases from cohort C to D for DBD (14.0%), DCD (169%), and total donors (33.8%) (Figure 2).

Discussion: Our experience demonstrates that a strategic vision to maximize donation can generate immediate growth as well as sustained growth over a period of years. The relative rates of growth for DBD and DCD are notable and appear consistent with shifting OPO donor demographics as well as evolving end of life practices. Technologies that increase the likelihood of DCD organs being transplanted such as machine preservation of livers, lungs, and hearts are future areas of focus for the OPO.

Global Kidney Exchange: Framework, Simulation, and Ethics For a Pilot Program

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Introduction: While the global burden of end-stage renal disease (ESRD) continues to escalate, access to kidney transplantation remains insufficient to meet the need. Global Kidney Exchange (GKE) responds to this growing public health crisis by matching willing, but incompatible donor-recipient dyads in an international chain of transplant procedures. Furthermore, GKE offers highly immunized patients (PRA>90) the rare opportunity for transplantation, providing improved quality of life and better clinical outcomes.

Objective: To simulate GKE structure and model as a pilot program for kidney exchange across three continents, discuss the ethical implications of a GKE program, and provide a cohesive structure for future GKE implementation worldwide.

Design/Methods: A simulated GKE chain of transplantations was identified using actual patient data from the United States (US) pool of the Alliance for Paired Kidney Donation, at a single point in time, supplemented by additional international pairs from Germany, Dominican Republic, and Italy. The research team identified virtual crossmatch negative matches and formulated a feasible financial framework based upon the different reimbursement rules and regulations of the different countries involved. Detailed logistics for the simulation of the chain are also described.

Results: The simulated transplant chain was initiated with a non-directed donor from the US and involved 8 donor-recipient pairs across four countries. The final bridge donor kidney was anticipated to be matched to a candidate on the US deceased donor waitlist. The transplant surgeries were planned to take place at pre-selected high volume transplant centers in either Italy or the United States. Logistics of organ procurement and transplantation were organized to align with the regulations of the countries where procedures were to be performed.

Conclusion: GKE is a feasible, equitable, and ethical method that facilitates worldwide kidney exchange and provides a conceptually sound way to match willing, but incompatible donor-recipient pairs. This program offers great potential to alleviate the morbidity and mortality of ESRD and narrow the gap between low access and high demand for kidney transplantation. GKE is a sustainable platform that leverages the financial savings and existing infrastructure of paired kidney transplants to unify healthcare systems to alleviate organ access disparities.

The First Independent Provincial OPO in China: Shanxi Experience

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Introduction: While the reform of organ transplantation in China has achieved success, the organ procurement model for different regions in the country varies. Starting from a hospital-based organ procurement organization (OPO), Shanxi OPO was established as the first independent non-profit provincial OPO in China, which covers a donation area of 37.29 million population and serves 6 transplant hospitals in the region. Shanxi OPO was established in 2018 under the supervision of Shanxi provincial health commission. This study compares results before and after the establishment in regard to the quantity, quality and efficiency of organ donation and transplantation (OD & OT) within Shanxi Province, aiming at exploring a feasible and up-to-date procurement management mode in China.

Method: From the point of organizational structure, personnel composition, equipment management and core quality indicators, we analyze the data from 2015 to 2021 and compare the results before and after the establishment of the provincial OPO.

Results: In the past two years, a professional team with 7 departments has been built. Besides, advanced facilities like those for donor maintenance and information collection are equipped. Then in 2020, an ethics and scientific committee have been founded to guide scientific research and supervise ethical norm compliance. Through analyzing the quality control indicators, the number of OD has increased from 35 cases (PMP: 0.99) in 2015 to 126 cases (PMP: 3.61) in 2021, with an increase rate of 260%. The growth trend remains within Shanxi Province even under the influence of COVID-19 pandemic in 2020, while the case number of the country decreased. Since 2018, the number of organs procured from per donor and the organ utilization rate of Shanxi OPO have risen year by year, reaching 3.02 and 98.7% respectively in 2021. Moreover, the DBD rate has increased from 1.1% in 2019 to 20.63% in 2021, though there is still a gap compared to the national and international level. These positive changes indicate that the quality of our service in organ viability assessment, donor maintenance, organ recovery and coordination have been gradually improved.

Conclusion: Efficiency and quality of the organ procurement and allocation have been greatly improved in the past few years because of the establishment of Shanxi OPO. This kind of provincial OPO also provides a solution, which will lead a clear direction for the standardization of organ procurement in China.
Impact of HLA-A,B DR and DQ on Living Kidney Transplant Outcomes in the Tacrolimus/MMF Era: An Artificial Intelligence Approach

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Introduction: One of the biological barriers that can impact outcomes among Living donor kidney transplantation is HLA mismatch. The aim of our study is to assess the effect of HLA mismatches on acute rejection rates and graft survival in the Tacrolimus era. Moreover, to assess factors affecting survival.

Methodology: All Living donor kidney transplant patients registered in UNOS database between 01/01/2005 and 01/12/2019 were retrospectively reviewed. Inclusion criteria: Living donor transplant recipients that were discharged on Tacrolimus/Mycophenolate Mofetil. Exclusion criteria: multiple organ transplants, previous kidney transplants, recipient age<18 years old, deceased donor transplants, missing data about induction therapy, missing HLA mismatch or ABO incompatible transplant. We used double-selection lasso (least absolute shrinkage and selection operator) logistic regression model to assess for acute rejection rates at one-year post-transplant. Variables of interest were HLA-A,B,DR and DQ mismatch. Variables Lasso selected from were: recipient characteristics (age, sex, BMI, ethnicity, diabetes, recipient/donor CMV status, pre-transplant dialysis), donor characteristics (age, ethnicity, diabetes and hypertension) and transplant characteristics (induction therapy, steroid intake, cold ischemia time, delayed graft function, PRA). Acute rejection was defined as biopsy proven or clinically suspected rejection. For survival analysis, we fit a penalised Cox model after choosing best alpha. Cross-validated grid-search was used to evaluate the best alpha. The variables included in the penalised cox model donor, recipient and transplant factors plus HLA mismatches.

Results: 28,736 patients were included in our study. Worse acute rejection rates at one-year post-transplant were noted with incremental increase in HLA-DQ (Two HLA-DQ: OR=1.29, P<0.01, 95%CI:1.08-1.54; One HLA DQ:OR=1.22,P=0.01, 95%CI:1.05-1.44), HLA-DR mismatches (Two HLA-DR: OR=1.85, P<0.01, 95%CI:1.48-2.31; One HLA-DR: OR=1.51,p<0.01, 95%CI:1.23-1.85), HLA-B mismatches (Two HLA-B OR=1.33, P=0.01,95%CI:1.05-1.69; One HLA-B match: OR=1.21,P=0.09) and HLA-A mismatch (OR:1.19, P<0.01). In the penalized cox regression model, None of the HLA types (A,B,DR or DQ) were associated with worse graft survival (P>0.05 for every type). The factors that were associated with worse outcomes are: Recipient black ethnicity (HR 1.2, P<0.01, 95%CI:1.10-1.31); delayed graft function (HR=1.54, P<0.01, 95%CI:1.31-1.81), pre-transplant dialysis (HR=1.19,P<0.01, 95%CI:1.12-1.26) and donor Black ethnicity(HR=1.21, P<0.01, 95%CI:1.10-1.33).

Conclusion: HLA-DQ, DR,B and A mismatches play a vital role in the occurrence of acute rejection among Living donor kidney transplant recipients. However, HLA mismatches have no significant effect on graft survival. Delayed graft function, pre-transplant dialysis recipient and donor black ethnicity, play an important role in determining graft survival.
401.2

Inhibition of Proprotein Convertase Subtilisin/Kexin Type A (PCSK-9) Among Renal Transplant Recipients: Is It Beneficial For Cases With High Cardiovascular Risk?

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Introduction: Reduction of low-density lipoprotein cholesterol levels is associated with reducing major cardiovascular events. Monoclonal antibodies inhibiting proprotein convertase subtilisin/Kexin type A (PCSK-9) have not been evaluated among renal transplant recipients despite its favorable safety profile.

Aim of the study: To evaluate the safety and efficacy of evolocumab in reducing lipids and cardiovascular events among risky renal transplant recipients.

Patients and methods: One hundred ninety-five kidney transplant recipients who were followed up in Hamed Al-Essa organ transplant center with high cardiovascular risk score (>20) were enrolled in this prospective randomized controlled study between June 2017 and June 2018. Patients who received statin and evolocumab (140mg/2 weeks, group 1, n=97) while those maintained on statin alone comprised group 2 (n=98). After 24 months, they were followed up clinically and by laboratory investigations.

Results: The two groups were comparable demographics, including pre-transplant co-morbidities (p>0.05). Before enrollment in the study, post-transplant complications were comparable to a higher prevalence of NODAT in group 2 (p=0.033). Smokers were significantly more prevalent in group 1. Moreover, basal graft function was significantly higher in group 1, while the type of immunosuppression was equivalent in both groups (p>0.05). Clinically we found no significant differences between the two groups concerning cardiovascular events, and both graft and patient outcomes were comparable (p>0.05). We found significantly higher basal cholesterol in group 1 (5.5 vs. 4.7, p<0.001), which came down significantly in the same group after three months and after that (p=0.031) compared to group 2 and basal values (p<0.001). Similarly, cholesterol started to lower significantly at 12 months in group 2. We observed that triglycerides in the two groups were comparable (p>0.05) till the end of the study. However, TG at six months was significantly lower compared to basal values in both groups (p<0.05). We reported 2 cases of acute MI and one atrial fibrillation in group 2.

Conclusion: Evolocumab is a promising lipid-lowering agent among kidney transplant recipients who are at high cardiovascular risk score. Earlier cholesterol reduction was observed in the add-on evolocumab group but without significant positive cardiovascular impact.

Keywords: Hyperlipidemia, renal transplant, high cardiovascular risk, outcome

Sisters working in the outpatient clinic of Hamed Alessa Organ transplant center of Kuwait: Shereen Mohamed, Bency Baby, and Sijy Paul.

401.3

Microvascular Inflammation in Renal Transplant Recipients Without Antibody Mediated Rejection

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Purpose: Microvascular inflammation (MVI) defined by glomerulitis (g) and peritubular capillaritis (ptc) is a hallmark of ABMR in renal transplantation. The prevalence and significance of MVI in patients without ABMR is less understood.

Methods: Here, we analyzed MVI in the first post-transplant year, its relationship to DSA, and its clinical significance in a large cohort of patients without ABMR. Along with any for-cause biopsy (fcBx), patients underwent 2 protocol biopsies (pBx, 3 & 12mos). Bx were categorized as early (0-4mos) or late (5-12mos). Serum was screened for DSA at 0, 1, 3, 6, 9 & 12mos post-transplant.

Results: MVI Prevalence: 956/1118 patients transplanted between 2013-18 underwent 1950 Bx (67% protocol, 33% for-cause). Of these Bx, 64 had either ABMR or GN and were excluded. MVI was noted in 23% (g+ptc score 1-1.5 in 13% & ≥2 in 10%) of the remaining 1887 Bx with greater prevalence in fcBx (fcbx 14% vs. pBx 7%) and late Bx (late Bx 29% vs. early Bx 17%). Of note, the MVI prevalence and its severity increased with increasing grades of tubulointerstitial inflammation (TII) (Fig 1A). Of note, 65% of patients with allograft infections (pyelonephritis & BKVN) had MVI. MVI & DSA: DSA was detected concurrently in 12% of all the 1887 Bx without ABMR. Although, MVI was associated with concurrent DSA detection in these Bx (OR 1.8, 95% CI 1.3-2.5, p<0.001), ~60% of the biopsies never had DSA (concurrent/historic or future). Furthermore, in biopsies stratified by the grade of TCMR, there was no significant difference in concurrent DSA detection between patients with and without MVI (Fig 1B).

Outcomes: MVI in patients without ABMR was associated with decreased 7yr-graft survival (Fig 1C, p<0.001). Importantly, the combination of MVI and TII was associated with worse graft survival when compared to either no inflammation or TII alone (Fig1C, p<0.001). Further, in a select sub-group of patients with allograft infection, MVI was associated with a trend towards decreased graft survival compared to no MVI (76% vs. 88%). Finally, MVI was associated with poor graft survival independent of potential confounders including DSA (HR 2.5, 95% CI 1.6-3.4, p<0.001).

Conclusion: MVI is common even in the absence of ABMR or DSA and is a marker for the severity of allograft inflammation and subsequent poor clinical outcomes.
Combined Genome Wide and Single Nuclei Transcriptomics in Posttransplant Acute Kidney Injury Identifies Early Proinflammatory/Profibrogenic Cell Origin

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Introduction: Kidney transplants offer a unique opportunity to evaluate molecular pathways involved in development and response to acute kidney injury (AKI) as most patients experience some level of AKI and graft biopsies are done frequently. This prospective study of transplanted kidneys with AKI investigates their unique transcriptomic profile and their role in chronic allograft dysfunction.

Methods: Fifteen AKI biopsies with histological features of acute tubular injury (pure-AKI) (collected within 1-month posttransplant) and paired 3-month protocol biopsies (n=30 biopsies) were assayed by microarrays. Normal allografts (NAs) biopsied at 3-months posttransplant were used as controls (n=20). AKI patients were subclassified based on their graft function (high/low) at 36-months posttransplant. A small subset of AKI samples (n=4) and NA (n=3) were evaluated using single nucleic(sn) RNA-seq to identify cells involved in injury or impaired reparation. Using the 10X Genomics Chromium Platform, >40,000 nuclei in Gel-Bead V3 were captured. Analysis of each dataset was generated with the CellRanger software and visualized using UMAP. Distinct cell clusters were identified by their expression of highly variable genes.

Results: DEGs (FDR<0.05) between pure-AKI and paired 3-month biopsies showed upregulation of the humoral immune response, neutrophil degranulation, and wound healing in kidney grafts with eventual low function at 36-months posttransplant. Gene enrichment analyses showed upregulation of epithelial mesenchymal transition, angiogenesis, and collagen formation in the same biopsies. Following snRNA-seq, 16 cell clusters were identified from pure-AKI and NA samples (UMAP displayed in Fig 1). Two types of proximal tubule cells were identified (PT1 and PT2) and characterized by decreased metabolic functions and SLC-mediated transmembrane transport in AKI grafts. The top up- and down-regulated PT biological pathways in AKI are shown in a heatmap in Fig 2. PT2 was characterized by dedifferentiation of PT. Three subsets of endothelial cells (EC1-3) were also identified. EC1 presented markers of glomerular capillary ECs. Fibroblasts presented an activated phenotype compared to NAs (extracellular matrix turnover, collagen biosynthesis). Proinflammatory monocytes were predominant in AKI samples.

Conclusion: DEGs between paired pure-AKI and 3-month biopsies associated with immune activation and impaired reparation in kidney grafts in allografts with low function at 36-months posttransplant. Critically, the analyses of transcriptional profile at single cell resolution identified early proinflammatory/profibrogenic cell subtypes. Further evaluation of cell subtypes and cell-to-cell interactions may lead to the discovery of targeted interventions to avoid progression to fibrosis and graft function loss.
Development of High-Performing and Multicenter-Validated Dynamic Prediction Models With Longitudinal Measurements of Serum Creatinine and Proteinuria for Death-Censored Kidney Graft Failure

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Introduction: Prediction models of graft survival in kidney transplantation allow risk stratification of kidney transplant recipients using big data and artificial intelligence. Many models require detailed information on allograft histology and presence of donor-specific antibodies which are not readily available in every transplant center. We developed a joint model using Bayesian estimation to correlate baseline transplant characteristics and longitudinal measurements of both serum creatinine (S-Cr) and urine protein-creatinine ratios (u-PCR) with death-censored graft failure (DCGF).

Methods: 3596 kidney transplant recipients (KTRs) from four transplant centers in Europe were included with a total of 452.033 S-Cr and u-PCR measurements. Each KTR had a median of 112 (IQR: 52-163) consecutive measurements. The interval between measurements was 7 (IQR: 1-35) days. Median follow-up was 6 (IQR: 3-9) years. Model predictors included recipient and donor gender and age, total number of human leukocyte antigen mismatches, donor type, pre-transplant DSAs, and dialysis vintage. Primary outcomes were DCGF six months after last S-Cr or u-PCR measurement and DCGF seven years post-transplantation. Two training and external validation methods have been used to assess best model performance: model 1; development in one center and validation in three remaining centers, and model 2; development on 80% of the total cohort and validation on the remaining 20% (Table 1).

Results: A total of 549 (15%) out of 3596 KTRs experienced DCGF. Joint modeling revealed that recipient age, recipient gender, donor age, transplantation after dialysis initiation, and serial measurements of S-Cr and u-PCR were independent risk factors for DCGF. Our final joint models showed good calibration (prediction error: 0.01) and very high discrimination in the development and validation cohorts (6-months incident AUC 0.9 [95% CI: 0.87-0.93] and 7-years dynamic AUC 0.84 [95% CI: 0.81-0.87] for model 1, and 6-months incident AUC 0.98 [95% CI: 0.96-1.00] and 7-years dynamic AUC 0.85 [95% CI: 0.80-0.91] for model 2) (Table 1). Especially model 2 could be of interest as a personalized surveillance tool in clinical practice given its AUCs >0.95 from year 1 onwards.

Conclusion: We developed a high performing and multicenter-validated, dynamic prediction model on death-censored allograft survival based on traditionally available baseline transplant characteristics and longitudinal measurements of S-Cr and u-PCR. This dynamic model can continuously be updated with new measurements and might enable personalized surveillance of kidney transplant recipients and objectify allograft prognosis (as illustrated in Figure 1). Of notice, our models can be extended with newly discovered dynamic biomarkers in the future if needed.
**Purpose:** Cytomegalovirus (CMV) infection is a threat to kidney transplantation. We studied circulating host proteome perturbations due to CMV infection in kidney transplantation as it could provide further insight on CMV infection and pathogenesis.

**Methods:** We performed LC-MS-based proteomics using 168 plasma samples collected pre- and longitudinally post-CMV viremia from 62 propensity score-matched UCLA kidney transplant patients of which 31 were CMV positive and 31 were CMV -ve. Recipients were sampled 3 and 12 months after transplant, with additional samples 1 week and 1 month after viremia. All data were log2 transformed for the analysis. Differential expression analysis was conducted by using R and Limma. T-tests were conducted by using the built-in statistics functionality in the R environment.

**Results:** Using Linear Discriminant Analysis, protein profiles with 241 plasma proteins were able to separate samples based on CMV viremia status and based on post-viremia time (Fig1A). Analysis of plasma proteins at the baseline pre-infection resulted in a set of 17 proteins whose levels were either increased (n=6) or decreased (n=11). The most significantly increased protein was Lysine Methyltransferase 2C (KMT2C) with 3.38 fold increase (p<0.0001) in CMV+ve samples and most significantly decreased protein was Immunoglobulin Lambda Variable 7-43 (IGLV7-43) with 2.17 fold decrease (p=0.01). The significant proteins were enriched in plasminogen activation and blood coagulation pathways as the top two biological pathways. The protein profile of baseline samples of CMV+ve patients was compared with protein profiles of 1-week post-viremia samples which resulted in ten significantly changed proteins (p<0.05). The significant proteins’ expression direction and significance are presented as a volcano plot (Fig1B). Increased proteins at the time of CMV+ve viremia (1-week post-viremia) included Serpin Family A Member 12 (SERPINA12) with p-value 0.01 and 2.47 fold increase and Immunoglobulin Heavy Variable 3-72 (IGHV3-72) with p-value 0.02 and 1.65 fold increase. Transthyretin (TTR) and Lysine Methyltransferase 2C (KMT2C), CMV-specific proteins were enriched with functions such as protein activation cascade (p=1.42E-06) and regulation of acute inflammatory response (p=0.0001).

**Conclusions:** We have identified plasma proteins that strongly correlate with CMV viremia in kidney transplantation and provide an insight about biological changes due to CMV viremia.

**Conclusions:**

1. The severity of fibrosis increased with the increase in transplant vintage with statistical significance (p <0.001).
2. The sensitivity was 85% and specificity was 67% in the differentiation of graft dysfunction with grade 2/3 IFTA from graft dysfunction with grade 0/1 IFTA obtained with cut-off value, 16.15 kPa.
3. The sensitivity was 85% and specificity was 67% in the differentiation of stable graft from graft dysfunction with moderate to severe fibrosis (cut-off value, 16.15 kPa).
4. The correlation of resistive index was insignificant when compared to the mean SWE score (r = 0.256, p = 0.007). There was a significant correlation between the Banff grade of IFTA and the mean SWE score, (p= 0.003).

**Conclusions:**

1. The correlation of resistive index was insignificant when compared to the mean SWE score (r = 0.256, p = 0.007).
2. There was a significant correlation between the Banff grade of IFTA and the mean SWE score, (p= 0.003).
3. The correlation of resistive index was insignificant when compared to the mean SWE score (r = 0.256, p = 0.007).
4. There was a significant correlation between the Banff grade of IFTA and the mean SWE score, (p= 0.003).

**Key words:** elastography, SWE, renal allograft biopsy, renal transplant, allograft fibrosis.
Dissecting the Impact of Molecular T-Cell HLA Mismatches in Kidney Graft Failure: A Retrospective Cohort Study

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Introduction: Kidney transplantation is the optimal treatment in end-stage kidney disease. Despite the growing understanding of the intricacies involved in rejection, de-novo donor specific antibody development continues to trouble patients undergoing kidney transplantation. One of the recent advances in solid organ transplantation has been the definition of molecular mismatch in Human Leukocyte Antigens (HLA). While not fully integrated in standard clinical care, cumulative molecular mismatch has shown promise in predicting transplant outcomes. Recently, however, our group has demonstrated that a subset of B-cell molecular mismatches (eplets) carry more risk than others. In this analysis, we sought to expand on our recent effort and study whether certain T-cell molecular mismatches (TcEMM) were highly predictive of death-censored graft failure (DCGF).

Method: We studied a retrospective cohort of kidney donor:recipient pairs from the Scientific Registry of Transplant Recipients (2000-2015). Allele level HLA-A, B, C, DRB1 and DQB1 types were imputed from serologic types using the NMDP algorithm. TcEMMs were then estimated using the PIRCHE-II algorithm. Multivariable models adjusting for donor, recipient and transplant characteristics assessed the association between single TcEMM and DCGF. Also, we fit multivariable LASSO penalized regression models to discriminate the TcEMMs most predictive of DCGF. To identify co-expressed TcEMM profiles, we applied weighted correlation network analysis (WGCNA).

Results: After applying the exclusion criteria, a total of 118,309 donor:recipient pairs were studied. We identified 1,935 unique TcEMMs between donor and recipient pairs at the population level by the PIRCHE-II algorithm. Each TcEMM was represented in 1 to 26,735 of the 118,309 pairs (median donor:recipient pair number of 1080). Models fitted to identify single TcEMM independently associated with DCGF found 218 such TcEMM. The LASSO penalized regression model identified an even smaller subset of 186 TcEMMs, of which 56 and 30 TcEMM were derived from HLA Class I and II, respectively, were statistically significant and deemed highly predictive of DCGF by the post-selection inference procedure. Since the co-expressed TcEMMs can serve as confounders, we also describe profiles of co-expressed TcEMMs.

Conclusion: In this analysis, we identified subsets of TcEMMs highly predictive of DCGF as well as profiles of co-expressed mismatches. Identification of these TcEMMs as determinants of immune injury could serve to inform allocation schemes and immunosuppression regimens with further experimental validation.

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Table: Clinical characteristics, biochemical and radiological parameters in the study population.

<table>
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<th>Parameters</th>
<th>Total</th>
<th>Allograft dysfunction</th>
<th>Stable allograft</th>
<th>p-value</th>
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<td>Age (years)</td>
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<td>BMI (kg/m2)</td>
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<td>Donor Age (years)</td>
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<td>Transplant vintage at time of scan (months)</td>
<td>22.8±17.45</td>
<td>24.4±19.86</td>
<td>20.3±12.84</td>
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<td>Serum creatinine (mg/dl)</td>
<td>1.7±1.17</td>
<td>2.0±1.39</td>
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<td>eGFR (CKD - EPI)</td>
<td>57.2±21.99</td>
<td>44.1±13.79</td>
<td>76.8±16.80</td>
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<td>Graft size (cm)</td>
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<td>Cortex thickness (mm)</td>
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<td>Skin to Graft distance (cm)</td>
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<td>Resistive index (RI)</td>
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<td>Parenchymal stiffness (kPa)</td>
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<td>16.5±15.42</td>
<td>14.2±8.50</td>
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Figure: Box and whiskers plot of point shear-wave elastography parenchymal stiffness (kPa) according to Banff grading of IFTA in patients with allograft dysfunction.

Figure: Grade 2 & 3 IFTA with Stable allograft AUC (AUC = 0.801; 95% CI: 0.682, 0.929; P <0.001)

ROC Curve

401.8

Figure 2: Grade 2 & 3 IFTA with Stable allograft AUC (AUC = 0.801; 95% CI: 0.682, 0.929; P <0.001)
Capnometry Values Are a Renal Transplant Evolution Predictor in Uncontrolled Cardiac Arrest Death Donors

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Introduction: The evaluation of a potential donor patient involves a series of tests and molecular markers to assess the suitability of an organ and the safety for the recipient. A fundamental marker used in out-of-hospital emergency medicine is capnometry, which allows us to indirectly, but accurately, evaluate the potential donor’s organs' perfusion. These values could help determine the adequacy of a possible donor in an uncontrolled non-heart beating donation (DACD) and donor selection during out-of-hospital medical emergencies. Capnometry values during cardiopulmonary resuscitation (CPR) are a renal transplant evolution predictor in DACD.

Method: Ours is a retrospective study of DACD Maastricht type IIa during a calendar year. The inclusion criteria of the study were: patients who have suffered a witnessed cardiac arrest; age between 16 and 60; asystole electrocardiographic pattern; less than 15 minutes until advanced life support (ALS) arrival; at least 20 minutes of CPR; less than 120 minutes until arrival at the hospital; absence of thorax and abdomen exsanguinating lesions; absence of suspicion of neoplastic, infectious diseases or intravenous drug users (IDUs); chest circumference compatible with chest compression system for donors; and being on hemodialysis and on the renal transplant waiting list for recipients. The data collected from the donors were: age, sex, body mass index, medical history, cause of death, CPR start time, ALS arrival time, time of arrival at the hospital, time of death, cold ischemia and warm ischemia time of each organ, and capnometry values at the beginning, at the middle point and at the end of CPR. As from the recipients, collected data were: transplanted organ, cause of chronic kidney disease (CKD), starting date of transplantation, number and type of transplant incompatibilities, renal failure, acute rejection, number of dialysis sessions after transplant, urologic complications, transplant-related infections, serum creatinine levels on 1st, 7th, 15th, 30th, 90th, 180th and 360th days after transplant, levels of proteinuria on 1st, 7th, 15th, 30th, 90th, 180th and 360th days after transplant, one-year transplanted organ survival, one-year recipient patient survival. The quantitative variables are summarized with their median and interquartile range (IR), and the qualitative variables are presented with their distribution of absolute (n) and relative (%) frequencies. We evaluated the correlation between capnometry values of the donor (at the beginning and at the middle point of CPR, and during hospital transference) with creatinine and proteinuria levels on the specified days using the Spearman correlation test. The association between qualitative variables with the capnometry values was evaluated with the Wilcoxon test. For all these tests, a p <0.05 was the accepted level of statistical significance.

Results: During a calendar year, 34 donors were studied. The mean age of the donors was 46.9 years, and 82.4% of them were male. The median capnometry value was: 21.3 +/- 12 at the beginning of CPR, 27.4 +/- 12.2 at the middle point of CPR, and 23 +/- 11.7 during hospital transference. The analysis of the correlation between at-the-middle-point-of-CPR and hospital-transference capnometry values, and creatinine and proteinuria levels, showed a statistically significant moderate-to-high negative correlation. Also, a statistically significant association was observed between hospital-transference capnometry values and the number of after-transplant dialysis sessions the receptor needed.

Conclusion: Capnometry is a useful tool to determine kidney transplant viability and prognosis. There is an association between donors capnometry values at the middle point of CPR and during hospital transference, and creatinine and proteinuria levels of the recipient, and another association between high capnometry values during hospital transference and a less need of after-transplant dialysis.

Membrane-Bound IL-2 Improves Expansion, Survival, Phenotype and Function of Car Tregs and Confers Resistance to Calcineurin-Inhibitors

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Introduction: Regulatory T cells (Tregs) play an important role in the maintenance of immune homeostasis and establishment of immune tolerance. Since Tregs do not secrete endogenous IL-2, they are especially dependent external IL-2. IL-2 deficiency leads to lower Treg numbers, instability of the Treg phenotype and loss of immune regulation. After organ transplantation, patients are treated with calcineurin inhibitors (CNIs) which further limits available IL-2. Application of low dose IL-2 expands Tregs, but also activates NK and CD8+ T cells. It was recently shown that graft-specific Tregs recognizing mismatched MHC I molecules via an chimeric antigen-receptor were far more potent in tolerance induction as compared to polyclonal Tregs.

Methods: We therefore aimed in amplifying transferred CAR-Treg function and stability by expression of a membrane-associated IL-2 (mIL-2). mIL-2 CAR Treg showed increased survival, better phenotypic stability and function as compared to CAR-Tregs currently used in clinical trials. They were also more stable under inflammatory conditions. In a preclinical humanized mouse model, we demonstrated that mIL-2 CAR-Tregs showed a better survival within the Treg niche than control CAR Tregs and were even resistant to CNI therapy with no effect on other Treg so mainly acting in cis. mIL2 CAR Treg were more effective than CAR Treg in preventing the rejection of allogenic targets in humanized mice.

Conclusion: The functional and phenotypic improvements of membrane attached IL-2 on CAR-Tregs will be an important step to enhance CAR-Treg therapies currently being tested in clinical trials after kidney and liver transplantation.
Successful Induction of Hematopoietic Chimerism by Dual Inhibition of MCL-1 and Bcl-2 Without Myeloablative Treatments in Nonhuman Primates

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Introduction: Induction of hematopoietic chimerism by donor bone marrow transplantation (BMT) is essential for achievement of allograft tolerance in clinical HLA mismatched kidney transplantation, while myelosuppressive toxicity of the radiation is yet to be solved. We have recently found that chimerism can be achieved with minimal total body irradiation in nonhuman primates (NHPs) by inhibiting Bcl-2 (anti-apoptotic protein) with Venetoclax (ABT-199). However, a minimal dose of TBI was still required for chimerism induction. Since Mcl-1, another member of the Bcl-2 family proteins, is highly expressed in hematopoietic stem cells (HSC) in bone marrow (BM), we hypothesized that Mcl-1 inhibition might delete the host HSC niche, thus facilitating donor bone marrow engraftment without TBI requirement.

Methods: HSC (CD34+CD90+CD45RA-) counts and Colony Forming Units (CFU) of BM aspirates were measured after treatment with ABT-199 (10mg/kg X 1) alone (n=3), Mcl-1 inhibitor (S63845, 5mg/kg X 5) alone (n=3), or combination of both (n=3). Three recipients treated with the combination underwent BMT from the MHC mismatched donor, and were also treated with ATG (3 doses pre-transplant) and anti-CD154 and a 28 day-course of cyclosporine (Fig. 1a). Another NHP underwent skin transplantation seven weeks after BMT with the same regimen including S63845 and ABT-199.

Results: Monotherapy of ABT-199 or S63845 depleted CD34+ BM cells to 50 ± 13% and to 42 ± 17% of pre-treatment levels, respectively. CFUs were also suppressed to 58 ± 8% and to 46 ± 17%, respectively. Combining ABT-199 with S63845 depleted more HSCs (22 ± 11%) with near complete depletion in two animals. CFUs were also effectively suppressed to 23 ± 8%(Fig. 1b). Since dual inhibition of both Mcl-1 and Bcl-2 most effectively depleted HSCs, BMT was performed using the combination of S63845 and ABT-199 (Fig. 1a). After conditioning, all recipients successfully developed multilineage chimerism, which lasted for 3 months, despite immunosuppression was completely discontinued at one month after BMT (Fig. 1c). Skin transplantation showed donor-specific tolerance with accepted donor skin graft and rejected two different third-party skin graft (Fig 1d).

Conclusion: Dual inhibition of Mcl-1 and Bcl-2 effectively depleted BM HSC, leading to successful hematopoietic chimerism induction without myeloablative treatments and donor-specific tolerance. This approach may set the path for the development of a novel and clinically applicable protocol for induction of hematopoietic chimerism without myeloablative treatments.

Investigating Iron Limitation in Tolerance and Regulatory T Cells’ Dynamic Iron Requirements

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Introduction: Pharmacological immunosuppression after transplantation increases morbidity and mortality, and thus alternative immunotherapies require investigation. Regulatory T cells (Tregs) are essential for maintaining immune tolerance and are great candidates for cellular therapy; understanding and modulating their function is therefore of formidable value. Iron restriction has been shown to impair effector T and B cell responses to vaccines and infections, but its effect on Tregs is largely unknown. A mutation in the transferrin receptor gene Tfr (Tfr2(Y20H)) leads to combined immunodeficiency in patients, caused by poor iron import via this transferrin receptor, but its effect on Tregs has not been studied.

Methods: Mice receiving fully mismatched skin grafts were injected with a hepcidin mimetic to lower serum iron, and Tregs from peripheral blood, spleens, and graft-draining or contralateral lymph nodes were phenotyped via flow cytometry. Treg phenotype was also assessed in a systemic infection model in malaria-infected Tfr(Y20H) mice. To study cell-intrinsic iron limitation in Tregs, RAG1- mice with a fully mismatched skin allograft were adoptively transferred with CD4+CD25+ conventional T cells (Tconvs) alongside CD4+CD25+ Tregs from either wildtype mice or iron-impaired Tfr2(Y20H) mice. Mixed wildtype and Tfr(Y20H) bone marrow chimeras were created for analysis of these mice’s immune composition and Treg phenotype, both at rest state and during skin transplant rejection. Cell-extrinsic and intrinsic hypoferremia in Tregs and Tconvs was also studied in vitro with activation, proliferation, migration, and suppression assays.

Results: Hepcidin mimetic injection impaired alloresponses in T cells and prolonged graft rejection, but Tregs seemed to be more resistant to iron limitation than Tconvs as shown by Tconv:Treg ratio, and Tregs even showed increased CD25 expression after hepcidin treatment. Similarly, Tfr2(Y20H) mice had impaired immune responses to malaria but Tregs were preferentially less impaired and better activated than other cells such as Tconvs. However, Tfr2(Y20H) Tregs were unable to control alloresponse when adoptively transferred, and migration assays with Tfr2(Y20H) Tregs suggest that this was not due to impaired migration to the graft. Mixed bone marrow chimeras are still in progress, but offer a direct comparison of wildtype and Tfr2(Y20H) Tregs within the exact same environment at steady state and after allo genetic challenge.

Conclusions: Tregs and Tconvs often differ in their metabolism or response to the same stimulus, and pathways that affect them differentially show great promise in tipping the immune balance toward tolerance or immune activation. These results on preferential Treg resistance to iron deprivation highlight iron as a candidate for manipulating the Treg:Tconv ratio, which could have tremendous therapeutic applications.
Expression of TNFR2 and CD29 Define a Highly Suppressive Subset of Human CD8+ Regulatory T Cells

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CD8+ regulatory T cells (Tregs) were the first suppressive cells reported in 1970, but they were put aside for years due to a lack of markers to properly define them. Our team demonstrated that CD8+ Tregs identified by low and/or negative expression of CD45RC, one of the isoforms of the CD45 molecule, show potent suppressive activity in vitro and in vivo, while cells expressing high levels of CD45RC do not. Herein, we addressed the heterogeneity within CD8+CD45RClow/-Tregs and identified new markers. We performed single cell RNA-sequencing on more than 10,000 non-stimulated CD8+CD45RClow/-Tregs subset as the most suppressed one cluster of particular interest expressing critical markers and molecules involved in tolerance. Using these technologies, we were able to characterize the transcriptomic heterogeneity at a single cell level and the proteomic heterogeneity from non-stimulated CD8+CD45RClow/- Tregs. We thus identified sub-populations of cells and one cluster of particular interest expressing critical markers and molecules involved in tolerance. Further work on two of these promising membrane markers, i.e., TNFR2 and CD29, using cell sorting and suppressive assays highlighted CD8+CD45RClow/-TNFR2low/CD29low Tregs as the most suppressive subsets within CD8+CD45RClow/- Tregs. Here, we reveal the importance of the combination of TNFR2 and CD29 as highly specific membrane markers for human CD8+ Tregs and highlighted their potential roles as targets for treatments in tolerance. Other new promising markers identified in our study showed an interesting role in CD8+ Tregs function; their precise roles are still under investigation. To date, to our knowledge, this is the largest characterization study of human CD8+ Tregs, this huge data resource will define them. Our team demonstrated that CD8+ Tregs identified by low and/or negative expression of CD45RC, one of the isoforms of the CD45 molecule, show potent suppressive activity in vitro and in vivo, while cells expressing high levels of CD45RC do not. Herein, we addressed the heterogeneity within CD8+CD45RClow/-Tregs and identified new markers. We performed single cell RNA-sequencing on more than 10,000 non-stimulated CD8+CD45RClow/-Tregs subset as the most suppressed one cluster of particular interest expressing critical markers and molecules involved in tolerance. Further work on two of these promising membrane markers, i.e., TNFR2 and CD29, using cell sorting and suppressive assays highlighted CD8+CD45RClow/-TNFR2low/CD29low Tregs as the most suppressive subsets within CD8+CD45RClow/- Tregs. Here, we reveal the importance of the combination of TNFR2 and CD29 as highly specific membrane markers for human CD8+ Tregs and highlighted their potential roles as targets for treatments in tolerance. Other new promising markers identified in our study showed an interesting role in CD8+ Tregs function; their precise roles are still under investigation. To date, to our knowledge, this is the largest characterization study of human CD8+ Tregs, this huge data resource will define them.

The Role of LAG3 in Antibody Responses to Kidney Transplantation

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The functions of co-inhibitory receptor lymphocyte activation gene-3 (LAG3) in T cells are well studied, however its role in humoral immune responses remains poorly characterized. The goal of this study was to test the role of recipient LAG3 in a mouse model of renal allograft rejection. Murine kidney transplant surgeries were performed from C3H (H-2Db) donors to B6 WT, LAG3−/−, CD4CreLAG3fl/fl & CD19CreLAG3 fl/fl recipients (H-2Dd) after bilateral nephrectomy. Grafts were evaluated by immunohistochemistry. WT recipients were treated with anti-mCD20 or anti-CD8 mAbs to deplete B cells or CD8 T cells, respectively. Immune responses were assessed by flow cytometry, ELISPOT assay, and serum levels of MHC-I and MHC-II-reactive IgG donor specific antibody (DSA) were determined by ELISA. Compared to WT animals, naïve B6.LAG3−/− mice have elevated numbers of CD44hi memory T cells, CXCR5hi follicular T cells, and B220+CD138+ plasma cells, and increased frequencies of memory CD8 T cells reactive to H-2Dd, H-2Dd, H-2Dd, and H-2Dd (Figure 1A) and elevated serum levels of IgG antibodies against H-2Dd, H-2Dd, H-2Dd, I-Ak, and I-Aa allotoligens (Figure 1B).

All C3H kidney allografts survived for >60d (n=5) in WT recipients, whereas recipient LAG3 deficiency led to rapid allograft rejection (MST of 14d, n=5) (Figure 2A) and elevated serum creatinine levels at d14 posttransplant. Compared to WT, LAG3−/- recipients had elevated frequencies of anti-donor IFNγ producing T cells and increased levels of DSA against MHC-I and MHC-II (Figure 2B). Graft histology at rejection revealed minimal T cell infiltration, diffuse C4d staining, atrophic peritubular capillaries, endothelial swelling and edema characteristic of antibody mediated rejection (AMR) (Figure 2C). Recipient CD8 T cell depletion did not alter rejection kinetics in LAG3−/- recipients (MST of 16d) (Figure 3A&B) and elevated serum creatinine levels at d14 posttransplant. Compared to WT, LAG3−/- recipients had elevated frequencies of anti-donor IFNγ producing T cells and increased levels of DSA against MHC-I and MHC-II (Figure 2B). Graft histology at rejection revealed minimal T cell infiltration, diffuse C4d staining, atrophic peritubular capillaries, endothelial swelling and edema characteristic of antibody mediated rejection (AMR) (Figure 2C). Recipient CD8 T cell depletion did not alter rejection kinetics in LAG3−/- recipients (MST of 16d) (Figure 3A&B) and, graft histological findings (Figure 3C) mirrored those of unmanipulated LAG3 deficient recipients (Figure 2C). Recipient CD8 T cell depletion did not alter rejection kinetics in LAG3−/- recipients (MST of 16d) (Figure 3A&B) and, graft histological findings (Figure 3C) mirrored those of unmanipulated LAG3 deficient recipients (Figure 2C). Recipient CD8 T cell depletion did not alter rejection kinetics in LAG3−/- recipients (MST of 16d) (Figure 3A&B) and, graft histological findings (Figure 3C) mirrored those of unmanipulated LAG3 deficient recipients (Figure 2C). Recipient CD8 T cell depletion did not alter rejection kinetics in LAG3−/- recipients (MST of 16d) (Figure 3A&B) and, graft histological findings (Figure 3C) mirrored those of unmanipulated LAG3 deficient recipients (Figure 2C). Recipient CD8 T cell depletion did not alter rejection kinetics in LAG3−/- recipients (MST of 16d) (Figure 3A&B) and, graft histological findings (Figure 3C) mirrored those of unmanipulated LAG3 deficient recipients (Figure 2C).
The Suppression of Macrophage-Mediated Intestinal Transplant Rejection by C5a Receptor Antagonist

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Background: Complement component C5a promotes alloreactivity via C5a receptor 1 (C5aR1) on immune cells. However, the role of C5a in small intestinal transplantation immunity has not been reported. During an inflammatory response, macrophages are activated by C5a and produce various inflammatory cytokines. In the present study, we examined the effect of the C5aR1 antagonist PMX53 on macrophage function following small intestinal transplantation.

Methods: We established models by heterotopic intestinal transplantation using donor Dark Agouti and recipient Lewis rats. The rats were administered PMX53 starting on the day of operation until postoperative day 7. We assessed graft survival and performed HE staining of grafts and mixed lymphocyte reaction tests (MLR) using mixed cultures of T cells from lymph nodes and spleen cells from donors. Based on the complement activation results, we estimated serum levels of C5a and C5 mRNA levels in the graft on postoperative day 6. We also evaluated macrophage and T cell accumulation in the graft. To verify antibody-mediated rejection, we estimated anti-donor-specific antibodies in serum. Finally, we assessed the effect of PMX53 on macrophage differentiation and activation using bone marrow-derived macrophages (BMDMs).

Results: Graft survival was significantly prolonged in the PMX53-treated group compared to that in the untreated group (6.6 vs 13.7 days, p<0.0001). PMX53 treatment inhibited shortening of the graft villus, as shown by the histological evaluation, and significantly lowered the stimulation index of the MLR when compared to the untreated group (2.2 vs 5.1, p<0.0001). In the untreated group, serum C5a and C5 mRNA levels in the graft were elevated. In the treated group, macrophages accumulation in the mesenteric lymph nodes of graft and monocytes in blood were reduced when compared with the untreated group (17.7% vs 7.9%, p=0.0007; 34.3% vs 20.7%, p=0.0005).

Anti-donor-specific antibody levels in the treated and untreated groups were similar (MFI: 144.5 vs 116, p=0.068). PMX53 treatment decreased BMDM differentiation (CD11b/c+RT-1b+ cell: 56% vs 30%, p=0.001) as well as IL-1β and TNF-α mRNA expression levels in activated BMDMs (181 vs 45.8, p=0.0001 and 15.1 vs 4.22, p=0.0055).

Conclusion: A C5a receptor antagonist suppresses rejection after small intestinal transplantation. Inhibition of C5a/C5aR1 signaling appears to regulate macrophage differentiation and activation.
404.7

Study on the Regulatory Effect of iPS-Derived Exosomes on the Local Immune Microenvironment in DCD Kidney Transplanted Rats

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Introduction: Ischemia reperfusion injury (IRI) of donation After Cardiac death (DCD) transplanted kidney is the key factor of acute renal injury, acute and chronic rejection of renal transplantation and transplanted kidney disease. The latest researches show that mesenchymal stem cells (MSCs) have the function of protecting damaged tissues and organs and strong immune regulation. Induced pluripotent stem (iPS) cells have higher proliferative capacity and exosome secretion potential than MSCs. In addition to the functions of stem cells, exosomes have the unique ability to cross the blood-brain barrier and deliver remotely, which means that exosomes have better advantages in clinical disease treatment compared with the therapeutic potential of stem cells. Therefore, the main purpose of this study is to clarify the role of IPS derived exosomes in protecting the IRI of DCD transplanted kidney and regulating its local immune microenvironment.

Methods: The iPS cells were passaged to the third passage and massively expanded. After 48 hours of culture, 100 mL of cell culture supernatant was collected and exosomes were extracted from the supernatant by the kit method, and the morphology and surface membrane marker proteins of the exosomes were identified. The SD rats were established with DCD renal transplantation model and 10, 50, and 100 μg of exosomes were infused into that SD rats respectively, and a PBS control group was set at the same time. On the 3rd, 5th, 7th, 14th and 28th days after transplantation, the content of cytokines in the serum of the recipient rats, the proportion of lymphocyte subsets CD4+CD25+Foxp3+Tregs in the spleen and the relative expression of Foxp3 mRNA were detected. The proliferation of renal tubular cells was detected by PCNA immunofluorescence. The pathological changes of renal tissue were determined by HE staining, and the apoptosis of renal tubular epithelial cells was detected by Tunel staining. The infiltration of inflammatory cells was detected by immunohistochemistry. The expression changes of regulatory T cells in renal tissue and macrophage phenotypic characteristics were analyzed by flow cytometry.

Results: The experimental amount of exosomes was successfully obtained, and the morphology was observed by transmission electron microscope. The exosomes were round or oval membranous vesicles with uniform size, and the edges were clearly visible. The TSG101, CD63, and CD9 proteins were highly expressed on the exosome membrane surface by western-blot. A DCD rat kidney transplantation model was successfully established. The expression levels of IL-12, IL-2, IFN-γ, and TNF-α in the serum of each group were increased to varying degrees from the 3rd day after operation. On the 3rd and 7th days, the levels of IL-12, IL-2, IFN-γ, and TNF-α in the 100 μg exosome infusion group were significantly lower than those in the 10 μg, 50 μg and PBS groups (P<0.05), and the expression level of IL-10 in the 100 μg exosome infusion group was significantly higher than those in the 10 μg, 50 μg and PBS groups (P<0.05). On the 28th day, the expression level of IL-10 in the 100 μg exosome infusion group was significantly higher than 10μg, 50μg and PBS groups (P<0.05). On the 28th day, the expression level of Foxp3 mRNA in the 100 μg infusion group was significantly higher than that in the 50 μg and PBS groups (P<0.01). Compared with other groups, the CD4+CD25+Foxp3+CD4 cells accounted for the highest proportion of CD4+ T cells in the spleen of the 100μg infusion group (P<0.05). On the 28th day, the expression level of Foxp3 mRNA in the 100 μg infusion group was significantly higher than that in the 50 μg group (P<0.05). The stainings of PCNA, HE and Tunel showed that SD rats infused with 100μg exosomes could significantly reduce the pathological damage, inflammatory response and apoptosis of renal tubular epithelial cells in the transplanted kidney, promote the proliferation of renal tubular epithelial cells, and have a protective effect on IRI kidney. On the 28th day, the expression of CD4+CD25+Foxp3+CD4 cells in the transplanted kidney tissue was significantly increased, which further promoted the differentiation of macrophages into the immunomodulatory M2 subset.

Conclusions: The infusion of IPS-derived high-dose exosomes is involved in the protection of the DCD kidney transplant during IRI process, and alleviates the acute and chronic injury of the DCD kidney transplant, and promotes the formation of the local immunosuppressive microenvironment in the DCD kidney transplantation.

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The Role and Mechanism of IFN-γ-Uc-MSCs-PEG2 Regulating MDSC Hypermethylation and Inducing Immune Tolerance in DCD Kidney Transplantation

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Introduction: With the widespread development of organ donation after cardiac death (DCD), the quality of organs has attracted more and more attention. The preservation time of DCD organs is significantly longer than that of living related donation, and the organic ischemia-reperfusion injury (IRI) is more significant. IRI is one of the main factors of chronic rejection in DCD-related kidney transplantation. The chronic rejection is an important cause of long-term failure of renal transplantation and the treatment is very difficult. During DCD kidney transplantation, an emergency response was initiated and inflammatory factors were highly expressed in vivo, especially the increase of IFN-γ. Umbilical cord mesenchymal stem cells (UC-MSCs) can rapidly inhibit the inflammatory response and secrete high concentrations of prostaglandin PGE2, which can mediate the hypermethylation of MDSCs to regulate the differentiation of M2 macrophages and their subpopulations. By injecting pre-sensitized UC-MSCs with IFN-γ, the method can inhibit or delay chronic rejection and induce specific immune tolerance while protecting IRI of transplanted kidney.

Methods: MDSC primary cells were prepared from fresh umbilical cord tissue, and the cells were passaged to the third passage (P3). The cell concentration was adjusted to 1×10⁵ cells/mL. UC-MSCs were pretreated with 100 ng/mL IFN-γ for 48 hours, and then transfused into DCD kidney transplanted C57BL/6 recipient mice, and three control groups were set up for observation. The peripheral blood, transplanted kidney and local tissues of the above-mentioned rats were isolated, and the expression abundance of PGE2 was determined by RT-PCR at the 3rd, 7th, 14th and 28th days after operation. The proportion, distribution, methylation and phenotypic changes of M2 macrophage cells and MDSC were also identified by single-cell sequencing technology. Pathological specimens were used to analyze T lymphocyte, neutrophil, and macrophage infiltration. Biochemical samples were used to detect the expression of inflammatory factors, oxidative stress (SOD, MPO, MDA), and the expression of apoptosis-related proteins (caspase-3, caspase-9, Bcl-2, Bax) in kidney cells were detected by western-blotting.

Results: The rat model of DCD kidney transplantation was successfully established. The hypermethylation status of MDSCs in the IFN-γ-Uc-MSCs kidney transplantation group was higher than that in the PBS and UC-MSCs groups (P<0.05). The abundance of PGE2 expression in the transplanted kidney and local tissue in the IFN-γ-Uc-MSCs group was higher than that in the other two groups. The ratio of M2/M1 macrophages was significantly higher than that in the other two groups (P<0.05). M2 macrophages were mainly distributed in the microenvironment around the transplanted kidney, and the phenotypes were dominated by M2b and M2c subtypes. From the 3rd day to the 7th day of transplantation, the expression levels of IL-12, IL-2 and IFN-γ cytokines in the serum of each group were increased. The increased levels of the IFN-γ-Uc-MSCs group and the UC-MSCs group were significantly lower than the PBS group (P<0.05). On the 14th day of transplantation, the serum level of IL-10 in the IFN-γ-Uc-MSCs group was significantly higher than other two groups (P<0.05). On the 28th day, CD4+CD25+ Tregs and CD4+CD25+Foxp3+ Tregs the spleen accounted for the highest proportion of CD4+ T cells, which was significantly different from other groups (P<0.05). Foxp3 mRNA expression in IFN-γ-Uc-MSCs group was significantly higher than that in UC-MSCs and PBS groups (P<0.05). The ratio of M2/M1 macrophages in IFN-γ-Uc-MSCs group was significantly higher than that in other groups (P<0.05). The HE staining of the transplanted kidney showed that the inflammatory response of the transplant was significantly lower than that of the PBS and UC-MSCs groups.

Conclusions: By injecting UC-MSCs pre-sensitized with IFN-γ, the DCD kidney transplanted rats can secrete a large amount of PGE2, which mediate the hypermethylation of MDSCs to induce an increase in the M2 macrophages. The increase of M2 macrophages forms a local immunosuppressive microenvironment, inhibit the occurrence of chronic rejection and induce long-term specific immune tolerance.
Experimental Assay of Intestinal Graft Viability and Function After Regional Abdominal Normothermic Perfusion

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Introduction: DCD has not been considered as a valid alternative for intestinal transplantation (IT). However, normothermia has recently improved the results of the classic cold-perfusion in other organs. Our aim was double: to test the viability and function of the intestinal grafts using normothermic regional perfusion (NRP) in an experimental porcine model and to assess ischemic-reperfusion injury (IRI) of the small bowel in human DCD.

Method: We used 8 donor-recipient pairs (25.5 ± 2.5 kg), supporting donors with an abdominal NRP. Their small intestine was heterotopically transplanted into the recipients. Blood and intestinal samples were obtained repeatedly throughout the procedure and 1, 2, 7 and 14 days after IT. IRI was evaluated using Park-Chiu score (PCS) in samples taken during NRP and up to 48 hours after IT. Samples from 7 and 14 days were analyzed to assess graft rejection and GVHD. The gene expression of TJP1, EPCAM, MUC2, LZY, IL-6, and TNF was measured in all samples. The absorptive function of the grafts was tested at the endpoint. Glycemia from the draining veins of the graft was compared with that from the native small bowel and peripheral blood 15, 30 and 60 minutes after intra-graft glucose administration. The small intestines from eight human DCDs were also sampled for histological analysis while other organs were procured for transplantation.

Results: All the intestines were successfully procured. One case was excluded due to venous stenosis. 6 animals (86%) reached the endpoint in good conditions. Grafts conserved architecture during NRP. The highest PCS was observed 1 hour after reperfusion, with denuded villi (PCS=4) in 3 samples (43%). All grafts recovered, with no or very subtle alterations after 48 hours. Five recipients (71%) did not show rejection signs at any time, 2 cases expressed mild rejection (29%) after 7 days. At the endpoint, one of them had recovered but the other had progressed to severe acute cellular rejection (14%). TNF-α, TJP1-1 and IL-6 showed maximum levels at the endpoint. Grafts’ glycemia reached its maximum 30 minutes after glucose administration, demonstrating their absorption capacity. Human samples did not show any IRI in 80% of the cases.

Conclusion: This experimental model postulates DCD with NRP as an alternative source of organs to address the mismatch between the waiting list for IT and the scarcity of donors. Its clinical and functional results appear to be comparable to those of other procurement techniques. The analysis of the human samples suggests that this approach could be successfully translated to the clinical setting.

The authors thank NUPA (Spanish Association of Help to Children and Adults with Intestinal Failure, Parenteral Nutrition and Multivisceral Transplant) and Fundación Mutua Madrileña for their support of the present research.


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Introduction: Pregnant patients with Short Bowel Syndrome (SBS) and chronic intestinal failure (CIF) can successfully reach to term their pregnancies while on Parenteral Nutrition (PN) but with high rates of complications. The availability of entero-hormones, especially semaiovamiglucagon like peptide 2 (sGLP2) has increased the chances to achieve intestinal sufficiency.

Case report: We report the case of a 33-year-old female patient with SBS/ CIF (anatomy type 2), weaned off PN using sGLP2. After 3.7 years of treatment, she became pregnant. The first decision was to interrupt the use of sGLP2 as pregnancy is a contraindication for its use. She was able to successfully carry out the pregnancy to term without any additional PN support. She had adequate weight gain (59.0 to 66.15 kgs); the newborn weight was 2,450 kgs, and she was able to breastfeed her without complications. Our initial hypothesis was that endogenous fetal GLP-2 (eGLP2) levels could have been a sufficient source to maintain an adequate maternal intestinal absorption, if able to cross the placental barrier. Thus, during the pregnancy, we decided to determine eGLP-2 levels in paired neonatal (cord blood) and maternal plasma samples from pregnant with (n=1) or without SBS (controls, n=2) during the partum and the immediate breastfeeding period (1 and 6 months postpartum); we also aimed to measure and compare eGLP2 plasma levels between pregnant (n=1) and a non-pregnant SBS patients (Anatomy type 2 (n=7); Anatomy type 3 (n=5)).

Materials and Methods: Blood samples were collected in ice chilled 10 ml tubes containing ethylenediaminetetraacetic acid (EDTA) and a specific dipeptidyl peptidase IV inhibitor. Plasma was immediately separated and stored at −80°C until analyzed.

Results: Our results indicated that eGLP-2 levels were significantly lower in neonatal than maternal plasma from our pregnant SBS patient compared to controls (Table 1). During postpartum, eGLP2 levels increased up to the six-month in both groups (Figure 1). Interestingly, our pregnant SBS patient showed significantly higher GLP-2 levels respect than controls (Figure 1) and non-pregnant SBS patients (Figure 2).

Conclusions: We observed that the endogenous neonatal GLP-2 does not represent an extra source of this entero-hormone to improve the adequate intestinal absorption during pregnancy in SBS patients. However, this study suggests that long periods of sGLP2 treatment in SBS patients could reach an effective intestinal rehabilitation sufficient not only to improve intestinal absorption (to carry out the full pregnancy and to sustain breast feeding), but also to probably increase the eGLP2 production. This study should be reproduced in experimental models and larger series to validate those results.

Table 1: GLP-2 (ng/ml) levels in pregnant SBS patient and pregnant women without SBS (control)

<table>
<thead>
<tr>
<th>Plasma samples</th>
<th>GLP-2 (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBS (n=1)</td>
<td>1.84±0.27</td>
</tr>
<tr>
<td>Control (n=2)</td>
<td>6.31±0.02</td>
</tr>
<tr>
<td>SBS vs. Control</td>
<td>1 month post-partum</td>
</tr>
<tr>
<td>6 months post-partum</td>
<td>10.4±0.72</td>
</tr>
</tbody>
</table>

Two-way analysis of variance.
Chronic Intestinal Failure Due to Short Bowel Syndrome in Adult Patients: 15 Years of Experience in Intestinal Rehabilitation at a Referral Center in Argentina

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Introduction: Chronic Intestinal Failure (CIF) due to Short Bowel Syndrome (SBS) is a complex disease that requires a multi and interdisciplinary approach in specialized centers. Although Parenteral Nutrition (PN) is the main support, long-time complications could be developed, and, some patients might require intestinal transplantation; but over the years, medical and surgical rehabilitation has become the cornerstone therapy allowing to achieve intestinal sufficiency minimizing the transplant need. Here we aim to assess the clinical and surgical characteristics of patients achieving PN independency by rehabilitation, at a single referral center.

Materials and Methods: A retrospective analysis from a prospectively fill data base including CIF/SBS patients was performed. Variables included were SBS etiology, intestinal rehabilitation surgery performed, post-surgical intestinal length, post-surgical anatomy type, time on PN and medical treatment implemented and Kaplan Meier analyses for PN independency and survival was done using SPSS v20.0.

Results: From 2006 to 2021, 368 adult patients with intestinal failure attended to our Unit; 264 of them (72%) had CIF and in 187 (71%) SBS, was the leading cause. One hundred and fifteen (62%) underwent AGIRS, and 84 (73%) were able to wean off PN after surgery. The mean post-surgical intestinal length in these patients was 155.3 ± 102.6cm and the post-surgical anatomy was type 1 in 3 patients (4%), type 2 in 22 (26%) and type 3 in 57 (68%). Overall mean time on PN for those patients weaned-off was 1,163 ± 4,488 days. Seventy-one patients (85%) achieve intestinal sufficiency with standard treatment (antisecretory, antimotility drugs) while other 13 patients benefit from using enterohormones. There was a significant difference in rehabilitation according to anatomy type (p= 0.001), intestinal length (p= 0.001) and treatment type (p= 0.001). Figure 1 and 2 show Intestinal rehabilitation according to anatomy type and intestinal length. Overall patient survival at 15 years was 89%. Only 19/368 patients required transplant (7%).

Conclusion: CIF/SBS are severe conditions that require a multidisciplinary team. Intestinal rehabilitation through medical-nutritional and surgical strategies have changed the outcome of this pathology. In our unit and, after 15 years of experience, intestinal sufficiency was achieved in patients despite having unfavorable intestinal lengths and anatomy types, becoming the main therapeutic approach, limiting the indications for transplantation.
Mortality on the Waiting List for Pediatric Patients Requiring Liver Containing Intestinal Grafts in Argentina, How Can We Reverse the Lack of Donors?

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Introduction: Pediatric patients requiring liver containing intestinal grafts have higher mortality on the waiting list compared to isolated intestinal transplant or pediatric liver transplant candidates. Major reasons being lack of young pediatric brain death donors (BDD). We aim to analyzed the mortality on the waiting list for pediatric recipients waiting for liver containing intestinal grafts.

Material and Methods: Retrospective analysis of all pediatric patients listed for combined liver-intestine or MTV, grouped as liver containing intestinal candidates (pLvCITx), and compared to pediatric isolated intestinal transplant (pITx) and cadaveric liver transplants (pLTx) between 2006 and 2022. Variables including: age, sex, time on the waiting list, mortality, drop-out or rehabilitation while in the waiting list, were analyzed. Number of pediatric BDD was analyzed by periods (2006-2013 (P1) and 2014-2021 (P2), and age group). SPSS v20.0 was used for statistical analysis.

Results: A total of 33 pLvCITx were included in the analyses and compared to 84 pITx and 1162 pLTx (table 1). The total number of pLvCITx in P1 was 8 and in P2 3, the number of IITX was 26 and 10 respectively; and the number patients who died on each list were: 5 and 6 for the pLvCITx; 4 and 4 for the pITx (p=N/S). The number of drop outs by periods for pLvCITx was: 5 and 1; while them were 10 and 3 for the pITx group.

There were 714 pediatric BDD, 207 younger than 10 years, and from them only 24 had less than 1 year; but 21 existed in P1, and only 3 in P2 (p=0.0035); similarly, for those between 1 and 5 years, there were 83, 51 in P1, and 32 in P2 (p=N/S). If deaths and drop-out are combined in the analysis, 48.5% of the pLvCITx, and 31% are at risk, vs 25% for the pITx (p=0.007). A higher number of pITx are able to improve while listed compared with the pLvCITx or pLTx. The 3-year KM survival on the waiting list for pLvCITx was 52%, being 81% for pITx, and 64% for pLTx (log rank: p=0.04).

Conclusions: Mortality in the waiting list remains higher for pediatric patients waiting for a pCLvITX; although pITx candidates had a higher drop-out while listed, that group has higher chances of improving or of being transplanted; and although donation remains low, it has become critical, and worsening in the last 7years for recipients below the year of age.
Long Term Results on Intestinal Rehabilitation of Children Treated at a Single Multidisciplinary Unit

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Background and aim: IF is a chronic condition with high morbidity. Intestinal rehabilitation can be enhanced when patients are treated by specialized multidisciplinary teams. We aim to show the long-term results of a group of children with SBS and chronic IF treated with a comprehensive approach at a single IF and transplant unit.

Material and methods: Retrospective review of a prospectively filled database of pediatric patients with chronic IF secondary to SBS (≤ 40 cm of remnant small intestinal length- RSIL) seen from May 2006 to December 2021. Patients were grouped according to the intestinal rehabilitation outcome; for survival analyses, late referrals were excluded. Data was analyzed using SPSS,v20.0.

Results: 67 patients were included; 46 (69%) male, 25 (37%) premature (mean gestational age 33.5 weeks), 55 (82%) had neonatal onset of IF. Etiologies were: gastroschisis (31%), intestinal atresia (22%), volvulus (19%), long segment Hirschsprung’s disease (7.5%), NEC (6.5%), post-surgical complications (5%) and others (9%). Median RSIL at the time of resection was 16.7±11.7 cm; intestinal anatomy type is shown in figure 1. Mean age at first consult was 2.93±3.51 years. At referral, mean time of PN dependency was 623±890 days, mean PN support 113% of the estimated basal metabolic rate for age. Fourteen (21%) had extensive central venous thrombosis and 16 (24%) had advanced fibrosis on liver biopsy. At the cut off day of analysis, 14 (21%) achieved intestinal rehabilitation, and 9 (13%) had at least 20% reduction of PN support. Twelve (32%) of those that remained PN dependent were included on the waiting list at referral and died shortly after thus are considered late referral. Fifteen (22.5%) underwent Intestinal transplantation (ITx) 14 Isolated, 1 MTV (figure 2). Ten-year conditional actuarial survival of the series was 72% (figure 3)(84% for PN dependent, 82% for rehabilitated patients and 57% for ITx recipients).

Conclusions: IR is possible even in very short gut or unfavorable anatomy when care is provided by a multidisciplinary team. Timely referral to specialized units results in diverse alternatives to reduce PN support and increases survival.

Figure 1 Intestinal Anatomy Type at referral

Figure 2 Patients grouped according to the intestinal rehabilitation outcome

Figure 3. Ten-year conditional actuarial survival
Worldwide Experience of 25 Years of Standardized Living Donor (LD) Intestinal Transplantation

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Introduction: ITX is performed in patients with irreversible intestinal failure requiring total parenteral nutrition (TPN) and TPN-associated complications. The vast majority of ITX are from deceased donors (DD). However, LD ITX has very specific advantages including elimination of waiting time, elective/pre-emptive surgery, shorter cold ischemia time, lower rejection rates and better HLA matching. It was not until 1997 that a standardized, effective, and successful surgical technique for LD ITX was introduced. This standardized technique has been used in most LD ITX since. The goal of this study was to investigate the current status and outcome of LD ITX.

Methods: A total of 85 LD intestinal transplants have been performed worldwide; 50 of them including 3 LD re-transplants were performed in the United States. Notably, there were only biological donors. The key principles of the 1997 standardized surgical technique for ITX are: (1) procurement of 180-200 cm of distal ileum in adults (about 60-150 cm for pediatric recipients based on age and weight), leaving > 65% of small bowel in the donor; (2) the terminal ileum (50-50 cm of the most distal ileum), the ileocecal valve, and the cecum remain with the donor to not interfere with B12-absorption, bowel transit time and bacterial flora; (3) the vascular pedicle comprises the ileocolic vessels or the terminal branches of the superior mesenteric vessels; the right colic artery is preserved; (4) bowel continuity after resection is immediately restored.

Results: Reliable patient and graft survival rates are available for primary US cases only (22 adult, 16 pediatric ITXs) based on mandatory UNOS reporting. For adult LD (vs DD) ITX recipients, 1- and 5- year graft survival rates were 64% and 41%, for pediatric transplant recipients 60% and 34%. There were no significant differences in patient and graft survival rates between LD and DD ITX (p>0.3). A major advantage of LD ITX has been that it was pre-emptively performed in some patients with advanced, but still reversible, TPN-induced liver disease, thus reducing the wait-list mortality for combined DD intestinal and liver transplants. There have been only 8 life-saving combined LD intestinal and liver transplants worldwide either simultaneously or subsequently; this procedure combines an adult left lateral liver lobe segmentectomy (segments 2 and 3) with the standardized LD intestinal transplant. 1-year graft survival for U.S. recipients of the combined procedure was 57% and there were no donor complications in any of the procedures.

Conclusion: Outcome of LD ITX: (1) The standardized surgical technique for LD ITX introduced 25 years ago is safe and reproducible; (2) Recipient outcome is not different for LD vs DD ITX; (3) No donor deaths or major donor complications have been reported; (4) Solitary LD ITX can be performed preemptively and reverse advanced TPN-induced liver fibrosis.

Noninvasive Biomarkers for Allograft Monitoring After Intestinal Transplantation: Promising Early Results From A Novel Peptide, REG3α.

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Background: The field of intestinal transplantation (ITx) lacks a specific biomarker for diagnosing acute rejection. Currently, calprotectin and citrulline, biomarkers used in monitoring disease activity in inflammatory bowel disease (IBD) and short-bowel syndrome, are employed for detection of allograft rejection. However, neither have proved their utility in distinguishing rejection from other non-specific causes of intestinal inflammation, giving these tests high sensitivity but low specificity and predictive value. The regenerating islet-derived (REG) proteins, a family of C-type lectin anti-inflammatory/anti-bacterial proteins expressed in Paneth cells within the epithelium of the small intestine, are emerging as a potential biomarker for intestinal pathology. Initially discovered in connection with pancreas islet regeneration in rats, REG proteins are known to be highly expressed in several human intestinal pathologies related to epithelial injury and inflammation. REG3α specifically has been correlated with disease severity in IBD and intestinal graft vs host disease (GVHD). While it shows potential as a biomarker for intestinal pathology, it has not been extensively studied in ITx.

Methods: Our center has maintained a detailed prospective database on all ITx recipients since 1991. A protocol of weekly allograft monitoring with stool calprotectin, serum citrulline and endoscopy with biopsy is followed. In 2015, REG3α was added to this protocol. Biopsy-confirmed acute rejection (BCAR) is graded according to international standards. Biomarkers are correlated to BCAR by post-operative week (POW). We compared biomarkers by severity of rejection (grade 0-2 vs 3-4) using standard statistical tests.

Results: Five adults underwent isolated ITx and one child underwent multi-visceral transplantation. Median time to first BCAR was 3 weeks; all experienced at least 1 episode of BCAR. One-year patient and graft survival was 100%. Calprotectin, citrulline and REG3α were significantly associated with grade 3-4 BCAR (p=0.00). The median REG3α level was 5.5 times the upper limit of normal during grade 3-4 BCAR. Calprotectin had the highest positive predictive value (PPV) (76%); REG3α had the highest negative predictive value (NPV) (89%). Together, they demonstrate a high PPV and NPV (100% and 93%, respectively).

Conclusions: This is the first case series to describe a protocol of allograft monitoring after ITx using invasive and noninvasive testing including REG3α. Calprotectin, citrulline and REG3α are individually associated with moderate-severe BCAR and together demonstrate a high PPV and NPV. REG3α demonstrates a superior NPV for detecting rejection. This preliminary experience indicates that REG3α may be useful as an ITx allograft monitoring. Ongoing efforts are aimed at conducting a prospective multicenter investigation to further determine the association of REGα with BCAR.

Table 1. Statistical Strength of Noninvasive Biomarkers in detecting Acute Rejection after ITx

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Mean (± SD)</th>
<th>Median (Range)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calprotectin (μg/g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none-mild (0/1/2)</td>
<td>77 (108)</td>
<td>44 (5-674)</td>
<td>0.00</td>
</tr>
<tr>
<td>moderate-severe (3/4)</td>
<td>119 (139)</td>
<td>394 (373-380)</td>
<td>0.00</td>
</tr>
<tr>
<td>Citrulline (μmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none-mild (0/1/2)</td>
<td>8 (16)</td>
<td>23 (4-69)</td>
<td>0.00</td>
</tr>
<tr>
<td>moderate-severe (3/4)</td>
<td>10 (35)</td>
<td>10 (4.18)</td>
<td>0.00</td>
</tr>
<tr>
<td>REG3α (ng/mL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none-mild (0/1/2)</td>
<td>406 (114)</td>
<td>406 (99-885)</td>
<td>0.00</td>
</tr>
<tr>
<td>moderate-severe (3/4)</td>
<td>143 (139)</td>
<td>143 (20-780)</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Normal values: *: <120 μg/g, **: 1-17.46 μmol/L, ***: >74.5 ng/mL
Preventing Encephalopathy After Isolated Small Bowel Transplantation Through Portal Graft Drainage

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Introduction: In isolated small bowel transplantation (SBTx), two methods of drainage have traditionally been described: systemic and portal. Although portal drainage (PD) is more physiological, allowing for the liver ‘first pass effect’, systemic drainage (SD) is often technically more feasible and has been shown in previous studies to have no significant side effects. In this single-centre study, we analyzed our experience over the years with both techniques.

Methods: We performed a retrospective analysis of our prospectively maintained data collected between 2007 and 2022. The following data was included in the study: age, gender, cause of intestinal failure, indication for transplantation, type of portal anastomosis (SD vs PD), infection rate, rejection rate, rate of encephalopathy and patient/graft survival.

Results: Between October 2007 and March 2022, 38 isolated SBTx were performed in 37 patients (n=15, 41%) males, median age 47 years (21-65). The most common indication was short bowel (n=32, 86%) with either impending loss of vascular access (n=10, 27%), IFALD (n=11, 30%) or a combination (n = 5, 14%). Twenty-six patient (68%) had SD, while 12 had PD (32%). PD drainage was performed with a venous jump graft in 10 patients and directly in 2.

Postoperatively, there were 12 patients (29%) with either transient or permanent encephalopathy (median ammonia level: 79 μmol/l (42-204)) and 8 patients (24%) with asymptomatic, raised ammonia levels (>30 μmol/l) but without clinical symptoms (38 μmol/l (34-64). All but one patient with clinical encephalopathy had SD. Median ammonia levels double in SD versus PD patients (71 vs 33.5 μmol/l; p=0.0076).

One patient underwent a conversion from a systemic to portal drainage due to severe, intractable encephalopathy using a third-party venous graft. This resulted in a complete reversal of her symptoms and normalization of her ammonia levels from 136 to <10 μmol/l). In three additional patients, conversion from systemic to portal is being considered. Conversely, two patients underwent portal to systemic conversion due to insufficient portal inflow.

Conclusion: Although, PD and SD yielded equal results in terms rejection and survival rates, encephalopathy was very frequent and occurred only after SD. Given this data, we advocate for PD whenever technically feasible, especially in patient with borderline liver function.

Drainage type

Peak Ammonia levels

![Diagram showing comparison of Peak Ammonia levels between Portal and Systemic drainage](image1)

**Peak Ammonia levels (μmol/l)**

- **Portal drainage**
  - Median ammonia level: 71 μmol/l
  - Range: 42-204 μmol/l

- **Systemic drainage**
  - Median ammonia level: 33.5 μmol/l
  - Range: 24-64 μmol/l

**Rejection-free Survival**

- Portal: 80% survival at 2 years
- Systemic: 70% survival at 2 years

**Patient Survival**

- Portal: 90% survival at 3 years
- Systemic: 85% survival at 3 years
Treatment of Complex Desmoid Tumours by Intestinal Transplantation

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Introduction: Desmoid tumours are rare, locally aggressive tumours which often have an unpredictable and variable clinical course. Although most desmoids (80%) are sporadic, 20% are associated with Familial Adenomatous Polyposis (FAP) which tend to be multi-focal and more aggressive. While the majority of desmoids can be managed by watchful waiting, systemic therapy or radiotherapy, some will require surgical excision. It is recommended in these cases to perform a total resection to reduce the chance of recurrence. In the most extreme cases (multiple segments of bowel, complex fistulating disease, invasion into the abdominal wall, ureteric encasement), the most radical option is to perform a total enterectomy and Intestinal Transplant (ITx). The decision if and when to refer a desmoid patient for ITx can be challenging, particularly the timing and sequence of treatment (simultaneous vs sequential exenteration + delayed listing for ITx). In this study, we present our centre’s experience of managing complex desmoid tumours with ITx.

Method: We performed a retrospective case review of our prospectively collected database between 2007 and 2022. All patients receiving an ITx for desmoids were identified.

Results: Between 10/2007 and 03/2022, 126 ITx in 119 patients were performed at our centre. Of these, 14 patients (12%) were for desmoid disease (6 Modified Multivisceral Transplants (MMVT), 5 Isolated ITx and 3 Liver-Small bowel Transplant. Median follow was 43 months (7-104). 9 out of 14 patients are alive (64%) without GI recurrence. None of the patients died from desmoid recurrence. The management of this cohort presented us with several complex technical issues that needed to be overcome such as loss of abdominal domain (6/14), retroperitoneal involvement (6/14), pouch related issues (2/14) and the need for a gastrectomy/duodenectomy due to dysplastic disease (6/14). Loss of abdominal domain and invasion/destruction by the desmoid disease was addressed by using non-vascularised rectus fascia (NVRF), either on its own (4/6) or in combination of vascularized muscle flaps (2/6).

Conclusion: Intestinal Transplantation is a viable treatment option in selected patients with extensive desmoid disease. Deciding which patients would benefit from ITx is important to ensure timely referral. Delays in this process can result in additional disease burden such as secondary liver disease or invasion of adjacent structures, requiring further reconstructions.

Retroperitoneal involvement of the vena cava/iliac vessels and the ureters. Two of these patients required a renal auto-transplantation into the iliac fossa.
410.1

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Introduction: Outcomes of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in kidney transplant recipients (KTR) compared with matched cohort is certainly lacking for different pandemic waves and geographic regions.

Methods: In this single-center retrospective study of coronavirus disease (COVID-19) cases admitted from 26 March 2021 to 7 June 2021, a propensity-matched analysis in a 1:1 ratio was performed to compare the clinical profile and outcomes between KTR and non-KTR. A Cox proportional hazard model from the whole study population to analyze risk factors for severe disease and mortality was calculated.

Results: We identified 1052 COVID-19 cases of which 107 (10.1%) were KTR. In propensity matched analysis, KTR had higher fever (81.6 % vs 60%; p-value = 0.01), lymphopenia (30% vs 11.7%; p-value = 0.02), higher neutrophil lymphocyte ratio (NLR) (43.3 % vs 25%; p-value = 0.05) and acute kidney injury (AKI) (66.6% vs 36.7%; p-value = 0.001). In Kaplan Meier survival analysis, there was no difference in mortality or severity of COVID-19. In cox hazard proportional analysis European cooperative oncology group score (ECOG) score of 1 to 2 (HR (95% Lower CI, Upper CI) = 4.9(1.8-13.5); p-value <0.01], ECOG of >2 [HR = 20(7.5,54.7); p-value < 0.01] and waitlisted status [HR = 1.9(1.1-3.3); p-value = 0.02] was associated with significant mortality. Kidney transplantation [HR = 0.8(0.47-1.44; p-value = 0.5] was not associated with mortality in the analysis.

Conclusions: In our report kidney transplantation status had a different spectrum but was not found independently associated with COVID-19 severity or mortality.

410.2
Outcomes of Living Donor Kidney Transplantation After SARS-CoV-2 Infection in Both the Donor and the Recipient: A Multicenter Study Running Title - LDKT in COVID-19 Survivors

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Introduction: The evidence for living donor kidney transplantation (LDKT) when both donor-recipient (D-R) pair had a history of COVID-19 infection is scarce.

Methods: We explored the protocol, outcome, and follow-up of 64 LDKT when D-R pair had recovered from COVID-19 in a retrospective, multicentre (n = 12) study from India between October 29, 2020, to December 1, 2021. There was no change in induction/immunosuppression regimen in the study among different COVID-19 severity and is similar to standard practice.

Results: Clinical severity in patients and donors was asymptomatic/mild without requiring oxygen therapy in 77%(n=49), 95.4%(n=63) and moderate/severe 4.6%(n=1) illness requiring oxygen therapy in 23%(n=15) and 4.6%(n=1), respectively. The mean ± SE(SD) waiting time from first documented RT-PCR negative to surgery for recipient and donor was 90.9 ± 9.27(74.1) and 47±4.5 (29.2) days respectively. Six (9.3%) episodes of biopsy-proven acute rejection (BPAR) were reported at follow-up of 214 ± 14.8(119) days and median (IQR) of 227(109-309) days. The locally weighted scatter plot smoothing curve for creatinine during follow-up in the D-R pair showed no trends of raised creatinine in the context of waiting time from COVID-19 to surgery. No graft loss, death, reactivation/reinfection, and any complications relating to surgery or COVID-19 were reported in the study.

Conclusions: Our report shows excellent outcomes and follow-up data of LDKT in recovered D-R pairs with the standard immunosuppression protocol. To date, this remains the first and the largest study of LDKT when D-R pair had prior COVID-19.
Quantifying Excess Deaths Among Solid Organ Transplant Recipients in the COVID-19 Era

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Introduction: Estimating the total COVID-19 mortality burden of solid organ transplant recipients (SOTRs), both directly through COVID-19 infection and indirectly through other impacts on the healthcare system and society, is critical for understanding the disease’s impact on the SOTR population.

Methods: Using national registry data from the United States, we modeled expected mortality risk per month pre-COVID (1/2015-2/2020) for kidney/liver/heart/lung SOTRs, and compared monthly COVID-era deaths (3/2020-3/2021) to expected rates, overall and among subgroups. Deaths above expected rates were designated “excess deaths”.

Results: Between 3/2020-3/2021, there were 3739/827/265/252 excess deaths among kidney/liver/heart/lung SOTRs, respectively, representing a 41.2%/27.4%/18.5%/15.0% increase above expected deaths (Figure 1). 93.0% of excess deaths occurred in patients age≥50. The observed:expected ratio was highest among Hispanic SOTRs (1.82) and lowest among White SOTRs (1.20); 56.0% of excess deaths occurred among Black or Hispanic SOTRs. 64.7% of excess deaths occurred among patients who had survived ≥5 years post-transplant. Excess deaths peaked January 2021. The geographic and temporal distribution of excess deaths broadly mirrored COVID-19 incidence (Figure 2).

Conclusion: COVID-19 likely caused over 5000 excess deaths among SOTRs in the US in a 13-month period, representing 1 in 75 SOTRs and a substantial proportion of all deaths among SOTRs during this time. SOTRs will remain at elevated mortality risk until the COVID-19 pandemic can be controlled.
Diagnosis of SARS-CoV-2 Infection and Impact on Subsequent 1-Year Patient Survival in Kidney Transplant Recipients – A Report of the Collaborative Transplant Study

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Introduction: It is well known that SARS-CoV-2 infections are associated with increased mortality in elderly people of the general population, but their impact on transplanted patients still needs to be investigated in depth. We analyzed patient survival in 2,135 kidney transplant recipients with a positive SARS-CoV-2 diagnosis and compared the outcomes to 2,135 matched kidney transplant patients without a SARS-CoV-2 diagnosis.

Materials and Methods: In 2020, the Collaborative Transplant Study (CTS) implemented a Covid-19 questionnaire used by 40 participating centers to send us information on diagnosis and vaccination status of kidney transplant recipients who were infected with SARS-CoV-2 (“infected patients”). We used the large CTS database to identify statistical siblings (“matched controls”) for each infected patient based on the following criteria: The matched control must have been transplanted at the same transplant center and around the transplant year of the infected patient (±5 years) and received the same donor type (living vs. deceased). For 2,135 of a total of 3,109 patients reported with a SARS-CoV-2 diagnosis, statistical siblings could be found. For each matched control, the respective survival time was adjusted by the time between transplantation and the SARS-CoV-2 diagnosis recorded for the corresponding infected patient. Demographics are shown in Figure 1. Multivariable Cox regression analysis was performed to determine the effect of SARS-CoV-2 diagnosis on subsequent 1-year patient survival using various confounders.

Results and Discussion: Kaplan-Meier analysis shows a significant impact of SARS-CoV-2 infection on subsequent patient survival (Figure 2). Overall, patients who were diagnosed with SARS-CoV-2 infection had a 6-fold higher risk of dying during the first year after diagnosis (HR=5.66, 95% CI: 4.59–6.98, P<0.001). Analysis of different subpopulations showed that the effect was similar for different geographical regions (Europe: HR=6.91, 95% CI: 3.74–12.76, P<0.001; South America: HR=5.48, 95% CI: 4.38–6.85, P<0.001), different age categories in years (<40: HR=6.16, 95% CI: 3.00–12.65, P<0.001; 40–59: HR=7.12, 95% CI: 4.97–10.21, P<0.001; ≥60: HR=4.94, 95% CI: 3.71–6.57, P<0.001), recipient sex (males: HR=5.30, 95% CI: 4.11–6.82, P<0.001; females: HR=6.85, 95% CI: 4.66–10.07, P<0.001). A preliminary analysis of our patient cohort did not reveal a significant protective effect of vaccination on mortality (HR=1.15, 95% CI: 0.89–1.47, P=0.28), but the number of available cases was small.

Conclusion: COVID-19 is commonly believed to affect mainly the elderly. However, our analysis of kidney transplant recipients showed that although higher absolute numbers of deaths were found among older patients, mortality risk associated with SARS-CoV-2 infection was increased in all age groups at a similar extent. Thanks to the ongoing support of the participating centers, the CTS is able to collect more data and will analyse them to confirm the results.
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The Impact of COVID-19 on Renal Function of Kidney Transplant Recipients: A Three-Month Prospective Study

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Purpose: This study aimed to assess changes in renal function during the acute disease and up to three months after the onset of symptoms among kidney transplant patients surviving COVID-19.

Methods: This ongoing single-center observational prospective study included kidney transplant recipients diagnosed between March 2020 and May 2021 and survived the first 28 days. Before diagnosis, baseline renal function was defined as the mean of the last three creatinine. The follow-up period was three months. We used a one-way ANOVA test to compare the mean eGFR in baseline, 28 days, and three months after COVID-19. The CKD-EPI equation was used to estimate GFR.

Results: Among the 787 patients, the mean age was 48.5 years, 59.3% were male, and 68.0% were white. Comorbidities such as hypertension, diabetes, and cardiopathy were present in 70.4%, 25.3%, and 3.9%, respectively. The mean body mass index was 26.9 kg/m², and baseline GFR was 51.9 ± 20.1 ml/min/1.73m². Immunosuppression was reduced by 27.1% and sustained in 9.5% of cases. In 30.3% of the patients, acute kidney injury occurred, 7.8% needed dialysis support, and 2.5% had graft loss. There was a decline in renal function at 28 days (50.0 ± 22.1 ml/min/1.73m²; p<0.001) and 3 months (47.3 ± 21.0 ml/min/1.73m²; p<0.001) after COVID-19. Among the patients, 47.3% did not return to baseline eGFR values within three months, and 19.9% reduced renal function at least 25%.

Conclusions: COVID-19 does impact early renal function decline in KTR. These data reassure that KTR represents a group that benefits from early access to effective preventive strategies.

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Background: Previous multinational studies of COVID-19 infections in kidney transplant recipients (KTX) from Asia suggest that the mortality rate is similar to that experienced in the West despite a younger population with less comorbidities. However, these studies were performed during the era where vaccination and better therapeutics for COVID-19 were not available. This multinational study from Asia seeks to determine whether mortality of COVID-19 infected KTX have improved with different eras in vaccination and therapies.

Method: Data of 657 KTX from 15 transplant centres in Singapore (n=196), Philippines (n=115), Mongolia (n=106), Malaysia (n=86), India (n=67), Bangladesh (n=53), Indonesia (n=21), Brunei (n=9), South Korea (n=3) and Hong Kong (n=1) were obtained to determine the effect of COVID-19 era (2022 vs. 2020-2021), country’s economic status according to the new World Bank country classification system, vaccination status (vaccinated vs. non-vaccinated), number of vaccine doses given (3 dose vs. 1-2 doses) and new COVID-19 therapeutics that are known to prevent disease progression (Remdesivir and SARS-CoV-2 monoclonal antibodies) on mortality from COVID-19 infection.

Results: Mortality from COVID-19 infection in KTX has improved over the last 3 eras (203.3% in 2020 vs. 16.7% in 2021 vs. 0% for first 3 months of 2022; P<0.005) and was lowest among high income nations vs. lower income nations in Asia (0.5% vs. 20.9%; P<0.005). Mortality among vaccinated KTX was lower than non-vaccinated KTX (5.1% vs. 32.4%; P<0.005) as well as among those who received 3 doses versus those who received 0-2 doses of vaccine 0.2% vs. 21.4%; P<0.005). There was no significant difference in mortality in KTX who received Remdesivir vs. those who did not (16.9% vs. 12.7%; P=0.128) but mortality was lower among those received SARS-CoV2 monoclonal antibodies (0% vs. 16.8%; P<0.005). On multivariate analysis, low income nation status was associated with higher mortality. These findings suggest that increasing vaccine doses and improving pandemic response capabilities of healthcare systems are important in reducing death from COVID-19.

Conclusion: This multinational study suggests that mortality has improved over time and with the introduction of COVID-19 vaccines and SARS-CoV-2 monoclonal antibody therapies. Receiving 3 doses of COVID-19 vaccine was associated with lower mortality while lower income nation status was associated with higher mortality. These findings suggest that increasing vaccine doses and improving pandemic response capabilities of healthcare systems are important in reducing death from COVID-19.
Crossmatch Positive Status Does Not Impact Long Term Outcomes in Simultaneous Liver Kidney Transplants

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Background: We recently examined the association between strongly positive crossmatch status and outcomes of simultaneous liver-kidney recipients (SLK)\textsuperscript{1}. Herein, we examine the association between positive crossmatch (XM) status of any capacity (weakly positive, T-cell, B-cell or both positive) and SLK outcomes in recipients discharged on a standardized immunosuppression regimen of tacrolimus and mycophenolate with or without steroids.

Methods: We analyzed the SRTR standard analysis file for all primary SLK recipients between 2003 and 2020 with available XM and induction regimen data. According to the XM status, recipients were grouped: crossmatch negative (XM-) N=3040 and XM+ (of any capacity) N=568. Kaplan-Meier curves were generated to examine recipient, death-censored liver and kidney survival by XM status. Cox proportional hazard models were used to investigate the association between XM status and outcomes of interest with follow-up censored at ten years. Models were adjusted for recipient age, sex, MELD scores, duration on the liver waitlist, induction immunosuppression, steroid maintenance, hepatitis C virus status, donor age and sex, local vs. shared organ status, liver and kidney cold ischemia time and previous liver transplant status.

Results: In the univariable analysis, XM status was not associated with recipient survival (log-rank p=0.59) or death-censored liver graft survival log-rank (log-rank p=0.014). Death-censored kidney graft survival, however, was slightly lower in the XM+ group (log-rank p=0.014). In the multivariable models, XM+ status was not associated with deleterious long-term recipient, liver graft, or kidney graft survival (p=0.78, p=0.15, and p=0.20, respectively). The 1-year liver rejection rate did not differ between XM+ and crossmatch negative (XM-) groups. The 1-year kidney rejection rate in the XM+ group was lower than their counterparts (4.6% vs. 9.1%, P<0.001), but the 1-year serum creatinine did not differ significantly between XM+ and XM- groups (p=0.23).

Conclusion: Although the kidney rejection rate is slightly higher in SLK recipients with XM+, the 10-year recipient, liver and kidney survival censored for death was not influenced by crossmatch status in the multivariable models.

Reference:
1. Riad S, Aby ES, Nguyen PL, Jackson S, Lim N, Lake J. Long-Term Outcomes of Crossmatch Positive Simultaneous Liver Kidney Transplants in the Unite. The data reported here have been supplied by the Hennepin Healthcare Research Institute (HHRI) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government.
Rejection After Liver Transplantation: What Can We Learn From Transcriptomic Analysis?

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Introduction: Acute cellular rejection (ACR) can occur at any time following liver transplantation (LT); initial ACR within 6 months is most common and occurs in up to 70% of recipients, with approximately 20% of patients experiencing one or more recurrent ACR episodes. Chronic rejection (CR) has been associated with increasing numbers of ACR episodes in some studies, and is the ultimate cause of graft failure in 15% of LT recipients. We sought to determine whether there were transcriptomic differences in ACR and CR after LT.

Methods: A total of 38 formalin fixed paraffin embedded (FFPE) liver biopsy specimens were included (9 normal liver tissue, 21 ACR, 8 CR). Specimens from recipients with HBV, HCV, or autoimmune hepatitis were excluded. RNA was isolated from FFPE sections, and gene expression was measured using the NanoString platform. Differential gene expression (DE) analysis and pathway analysis (PA) using the KEGG database were performed, with Benjamini Hochberg p-value correction for false discovery rate.

Results: There were significant differences in DE between ACR and normal liver tissue (Figure 1A, 142 genes), and in PA there was significant upregulation of genes involved in the common rejection module (n=4 genes) and antigen processing and presentation in ACR versus normal (n=15 genes, p<0.001). Similarly, there were significant differences in DE between CR and normal (Figure 1B, 145 genes) and PA showed significant upregulation of genes involved in antigen processing and presentation (n=6 genes) and allograft rejection (n=6 genes). In DE comparing ACR and CR, significant differences in 28 genes were identified (Figure 2A), with PA demonstrating small differences in a variety of immunologic pathways (Figure 2B).

Conclusions: Compared with normal liver allograft biopsies, both acute and chronic rejection show significant enrichment of pathways associated with allograft rejection and antigen processing. Only acute rejection showed overexpression of genes present in the common rejection module. Our hope is that these findings will serve as the foundation for identifying unique pathways associated with chronic rejection leading to better or novel strategies for immunotherapy.

Preoperative Cystatin C Predicts Acute Kidney Injury Following Liver Transplantation in Patients With Normal Serum Creatinine

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Introduction: Serum creatinine (Creat) is not a reliable marker of renal function in patients (pts) with cirrhosis mostly because it is highly influenced by several extrarenal factors. In contrast, recent studies showed that cystatin-C (CystC), a renal biomarker produced by all nucleated cells, is a more sensitive marker of decreased GFR than Creat and a good predictor of hepatorenal syndrome. Postoperative acute kidney injury (AKI) increases morbidity and mortality of liver transplantation (OLT). The goal of this study was to evaluate preoperative Cystatin C levels as a predictor of post-OLT AKI in adults with cirrhosis.

Methods: Prospective study including consecutive pts transplanted in two centers from 2019 to 2021. CystC (immunoturbidimetric assay, normal 0.4-0.99 mg/dL) and Creat (mg/dL) were determined upon admission for the transplant and within 12 hours of surgery. Preoperative Cystatin C levels as a predictor of post-OLT AKI in adults with cirrhosis.

Results: The study included 131 pts aged 52±12.5 years (61% males). HCV was the most frequent etiology of cirrhosis (24%) and 35% of pts had hepatocellular carcinoma. Pre-OLT Creat was 0.85±0.42 mg/dL, Cys 1.46±0.46 mg/dL and MELD-Na 20±8. Increased serum Creat was observed in 15/131 pts (11.4%). In contrast, 66/131 pts (50.4%) had CysC values >1.1 mg/dL (p<0.001). Among the 66 pts with elevated CysC, 39/66 (59.1%) develop AKI compared to 18/65 (27.7%) with normal CysC (p<0.001). Independent predictors of post-OLT AKI on multivariate analysis were CysC >1.4 (OR 3.47 95% CI 1.35-9.52, p=0.011) and elevated Creat. No deaths occurred before the primary endpoint of the study. The incidence of postoperative AKI was 43.5% (57/131). Among patients with elevated CysC, 39/66 (59.1%) develop AKI compared to 18/65 (27.7%) with normal CysC (p<0.001). Independent predictors of post-OLT AKI on multivariate analysis were CysC >1.4 (OR 3.47 95% CI 1.35-9.52, p=0.012), BMI>30 (OR 3.08 95%CI 1.2-8.43, p=0.024), red blood cell transfusions >5 units (OR 5.93 95%CI 1.65-24.8, p=0.011) and preoperative hipoalbuminemia <2.5 gr/dl (OR 3.96 95%CI 1.39-12.1, p=0.012).

Conclusions: A large proportion of OLT candidates with cirrhosis and normal Creat have elevated levels of CysC which appears to be a better marker of renal dysfunction in this patient population. Preoperative CysC, but not Creat, was a potent predictor of post-OLT AKI. Early preoperative identification by CysC of pts at risk of post-OLT AKI may play an important role at the time of selecting the immunosuppressive regimen, using either induction or nephroprotective agents.
Molecular Characterization of Progressive Fibrosis in the Liver by Single-Nuclei RNA Sequencing

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is associated with an increase in inflammatory processes which potentially contribute to the exacerbation of fibrosis and development of cirrhosis. Hereby, we assess the use of single-nucleus RNA sequencing to identify the molecular mechanisms by which NAFLD progresses towards fibrosis at the single-cell resolution.

Methods: Single nuclei isolated from flash-frozen samples included normal, NAFLD, non-alcoholic steatohepatitis (NASH), and cirrhosis. Isolated nuclei were processed through a 10x Genomics Chromium Platform and analyzed via the Cell-Ranger pipeline. The Seurat package was used to generate clusters and cell identification. Cell types were analyzed for differentially expressed genes, which were further characterized by the predictive subcellular localization of the associated translated protein. Gene sets predicted to localize to the nucleus, cytosol, and mitochondria were individually explored for KEGG/GO-term enrichment and pathway analysis.

Results: Four hepatocyte (HEP) clusters and two hepatoblast (HpB) clusters were identified. HEP-1 and HpB-1 were found to be expressed almost exclusively in NAFLD. Gene clusters associated with mitochondria-localized gene products within the HpB-1 cell type were enriched for GO-terms specific to fatty acid oxidation and an upregulation of reducing power. In contrast, the HEP-1 cell type was found to have an increased reliance on amino acid metabolism, specifically the catabolism of branched chain amino acids by the upregulated activity of MCCC1, DBT, and HIBCH. In addition, gene clusters predicted to localize to the cytosol within the HEP-1 cell type were enriched for pathways specific for cellular response to oxidative stress. Taken together, these findings would suggest a progression of metabolic dysfunction from HpB-1 to HEP-1. In addition, these two cell types were also found to have a significantly higher concentration of genes associated with ECM production, including TIMP3, MMP15, ECM2, C1QTNF3, and SERPINE1.

Conclusion: In this study, we identify two cell types exclusively found in NAFLD which show an upregulated response to oxidative stress and fibrogenic mechanisms in light of progressive metabolic dysregulation. With continued progression, onset of fibrosis lends to the eradication of hepatocytes and replacement of epithelial cells with fibrotic cells, thereby highlighting the cellular shift from NAFLD to Cirrhosis.
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Autophagy Mediates Liver Functional Recovery From Donation After Circulatory Death Rats With Normothermic Machine Perfusion

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Background: Liver transplantation from donors after cardiac death (DCD) has been a routine treatment for end-stage liver diseases. Normothermic machine perfusion (NMP) could be beneficial for the function recovery of DCD livers. The mechanism of NMP is still unclear. The purpose of the study was to investigate the molecular changes and the underlying mechanism of liver recovery with NMP.

Methods: The SD rat livers were subjected to 30 warm ischemia after cardiac arrest and thereafter stored for 8h under cold static preservation, which was harvested and regarded as Group cold static (Group CS, n=6). In experimental groups, livers received an ex vivo dual NMP without an autophagy inhibitor (Group NMP, n=6), 3-methyladenine (3-MA), or with (Group 3-MA, n=6) in the perfusate for 2h. Perfusates were harvested to detect hepatic enzyme activity and liver samples were harvested to detect the expression of autophagy-related proteins Atg7, Beclin-1, LC3, and liver function. Comparative proteomic analysis was performed using an integrated approach involving LC-MS/MS analysis and Tandem Mass Tag labeling.

Result: Compared with Group CS, lower hepatic injury of Group NMP was characterized by a lower change of liver enzymes and a better histological evaluation. Proteomics indicated that a total of 294 differentially expressed proteins were identified with 196 up-regulated proteins and 98 down-regulated proteins in NMP livers compared with Group CS. There were notable differences in the expression of autophagy-related proteins between Group NMP and Group CS. Additionally, NMP pretreatment increased the ratio of LC3-II/LC3-I, the expression of Beclin-1 and Atg7 based on Western blot than Group CS. The autophagy inhibitor upregulated perfusate aminotransferases and increased the Suzuki score.

Conclusion: NMP can decrease hepatic ischemia-reperfusion injury and may confer better protection against liver damage from DCD. Autophagy may participate in liver functional recovery from DCD with NMP, indicating that liver autophagy might be a key therapeutic target for rehabilitating the function of DCD.

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Inferior Long-term Outcomes of Simultaneous Liver-Kidney Transplantation Using Donation After Cardiac Deaths Donors in the United Network for Organ Sharing Database

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Background: Outcomes of simultaneous kidney-liver transplantation (SLKT) in donation after cardiac death (DCD) have improved over the years, but data are limited. Aim of this study was to assess the long-term outcomes of SLKT from DCD organs and then compare them to donation after brain death (DBD) organs.

Methods: We analyzed data from the United Network for Organ Sharing (UNOS) from 2002 to 2021. Adult SLKT were included, other multi-organ and re-transplants were excluded from the analysis. Propensity score matching was performed to assess the outcomes between two groups. P<0.05 was considered as significant.

Results: In the United States, 8733 SLKT were performed during the study period (499 SLKT from DCD and 8234 from DBD). Recipients of DCD organs, when compared to recipients of DBD organs, were older (median age 59 vs 58 years, P=0.005), had lower prevalence of diabetes (62 vs 68%, P<0.005), and were more likely to have worse Model for End-Stage Liver Disease (MELD) score (24 vs 29, P<0.001) and longer wait-time (89 vs 68 days, P=0.009). Donors of DCD organs were younger (median age 33 vs 35 years, P=0.001), had shorter cold ischemia time in liver (5.8 vs 6.0 hours, P=0.001) and in kidney (9.5 vs 10.5 hours, P=0.001), and had similar kidney donor profile index (31 vs 30%, P=0.18) compared to DBD donor. The most common primary diagnosis for both recipient groups was alcohol-related liver disease, while non-alcoholic steatohepatitis was more common in DCD group (29 vs 21%). Long-term outcomes including five-year overall survival and liver graft survivals were inferior in DCD recipients (71.4 vs 74.8%, P=0.01; 74.0 vs 67.1%, P=0.0011). After propensity score matching, five-year overall survival and liver graft survivals were inferior (71.4 vs 76.4%, P=0.031; 67.1 vs 76.0%, P=0.001). Multivariable cox-regression analysis in the matched-cohort showed that DCD was an independent risk factor of mortality (hazard ratio (HR)-1.32; 95% Confidence interval(CI), 1.04-1.68; P=0.021) and liver graft failure (HR-1.54; 95% CI, 1.24-1.92; P=0.001). For kidney allograft outcomes in matched-cohort, delayed graft function was higher in DCD (36 vs 20%, P<0.001) and five-year kidney graft outcome was inferior in DCD (67.3 vs 74.7%, P=0.0034). The most common listed causes of five-year mortality were infection (21.4%) and multi-organ failure (20.8%) and there were no differences between two groups. Other factors associated with mortality were recipient older age (HR 1.03; 95%CI 1.02-1.04, P<0.001), male recipient (HR 1.32; 95% CI, 1.06-1.64, P=0.014), and donor older age (HR 1.01; 95%CI 1.00-1.02, P=0.024).

Conclusion: Recipients of SLKT from DCD donors had inferior long-term post-transplant outcomes with decrease in overall survival and allograft survival. Careful identification of risk factors associated with worse outcomes is required to improve utilization of DCD donors for SLKT.
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Lip Actinic Cheilitis and Its Relationship to Clinical Characteristics and Immunosuppression in Kidney Transplant Recipients

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Introduction: Due to drug immunosuppression after kidney transplantation (KT), as well as factors such as chronic uremia and chronic sun exposure, Kidney Transplant Recipients (KTR) have a 46-fold increased incidence of Lip Cancer (LC). Because of the high prevalence of LC in KTR, there are concerns about its prevention, which can be accomplished by diagnosing Actinic Cheilitis (AQ) on lips, a potentially malignant oral lesion that can progress to LC.

Aim: The purpose of this investigation was to see if there was a link between the clinical manifestations of AQ and the clinical profile of KTRs.

Methods: Convenience sampling in a cross-sectional observational clinical study. An expert researcher completed the diagnosis and clinical staging of AQ in KTRs using Pointevin et al 2017 criteria and a clinical evaluation and photographic record of six different angulations of the lower lip were used to calibrate the researcher (Kappa intra-avaliador >0.8). Demographic data, time since KT, immunosuppressants, exposure to AQ risk factors such as alcoholism, smoking, chronic sun exposure, and exposure to volatile chemical agents, and history of positive serology for oncogenic viruses after KT were all obtained retrospectively from electronic medical records. For the association of variables, Chi-square and Macnemar tests were performed, with a significance value of (0.05).

Results: The sample size was 48 (100%) KTR, with 29 people diagnosed with AQ (60.41 percent). Light-skinned KTR was linked with the most severe AQ staging in 9 subjects (18.75 percent; p=0.035). History of exposure to volatile chemical agents (16.33 percent; p=0.007), drunkenness (15.25 percent; p=0.008), and smoking (20.66 percent; p=0.05) were also risk factors for AQ. A history of prolonged sun exposure was linked to a higher severity of QA: 22 (45.83 percent; p=0.001). The prevalence of AQ was linked to the usage of tacrolimus 43 (89.58 percent; p=0.016) and azathioprine 11 (22.91 percent; p=0.001). However, the use of Mycophenolate Mofetil was linked to the most severe cases of AQ in 7 patients (14.58 percent; p=0.05). Individuals who got sirolimus, on the other hand, showed less AQ expression, with 7 patients (14.58 percent; P=0.016) manifesting with lesser degrees. After TxA, positive Epstein-Barr Virus serology was linked to the existence of AQ 17 (35.41 percent; p=0.028).

Conclusion: The presence and severity of AQ in KTR were linked to fair skin, chronic sun exposure, Epstein-Barr Virus infections, and the use of Mycophenolate Mofetil. Sirolimus appears to have a protective effect against the development of AQ. It is possible to select groups of patients at higher risk for AQ and, as a result, for LC using this clinical profile associated with the manifestation of AQ, allowing for prevention and early diagnosis.

This study was approved by the Ethics and Research in Human Beings Committee under protocol CAAE12798019.3.0000.5417.

412.2

High Intrapatient Variability Tacrolimus’s Levels Is Associated With Post-transplant Diabetes Mellitus in Kidney Transplant, A Mexican Cohort

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1Nephrology and Transplant, Central Military Hospital, Mexico city, Mexico.

Introduction: Porrini E showed that tacrolimus represents a risk factor for post-transplant Diabetes Mellitus (PTDM) development, increasing prediabetes incidence by 33% 1 year post-transplantation. Several mechanisms have been implicated in the association of calcineurin inhibitor and PTDM: decreased insulin secretion, glucose intolerance, reduced pancreatic beta cell mass and decreased insulin gene expression. DIRECT study (Diabetes Incidence after Renal Transplantation) showed the incidence in 73 CsA patients (26%) and 96 Tac patients (33.6%, p = 0.046). By the other side, Malik RF et al mention that FK levels isn’t a risk factor for the development of PTDM.

Method: A retrospective study was performed. All patients who received living or deceased-donor kidney transplant in the study period 2002 to 2020 was included and measured Tac/CsA and glucose level at months 0,3,6,9, and 12. Hb1Ac was also determined at 6 and 12 months. Patients who did not have at least 12 months post-transplant follow-up were excluded. PTDM diagnosis was made according the American Diabetes Association (ADA). Intrapatient Variability (IPV) coefficient was estimated by calculating the CV according to the following equation: CV (%) = (SD/mean Tac trough concentration) x100. Mean concentrations were calculated using all outpatient Tac concentrations between 1 and 12 months. Recipients were separated into 2 groups, low IPV and high IPV, according to the CV cutoff= 37.31% (which is CV median value in the whole cohort).

Results: 640 patients were included; 69.4% were transplanted from living related donors; most frequent CKD etiologies were ND and CNG with 33.3%, 30.3% respectively. 64.4% of the transplant recipients were induced with Basiliximab and 1-year postransplant time, 463 patients (72.3%) were on tacrolimus as maintenance immunosuppression and 27.7% on CsA. The mean age recipients was 38.32 (±13.66) years old. Cr mean 1-year postransplant time was 1.39 (±1.19) mg/dL. There were no statistical differences in mean oral steroid dose between groups. Mean levels FK and CsA were 12.41 (±5.31) and 234.34 (±87.80) ng/mL and 9.13 (±5.3) and 194.38 (±92.44) ng/mL in the PTDM and without PTDM groups, respectively (p >0.05). 116 patients did met PTDM criteria (18.1%) within first year after transplantation; 55.1% patients were treated with metformin and 33.6% patient with basal insulin. Patients who had tacrolimus high IPV coefficient developed higher PTDM than those with low variability with statistically significant difference (43.22% vs 29.99%, p=0.05). The student’s t test value to compare the IPV was 0.03; ANOVA p= 0.00. Our PTDM incidence was lower than other hispanic multicenter cohort.

Conclusion: High IPV tacrolimus’s levels proved to be another risk factor for the development of PTDM. The use of prolonged-release medications can be a measures to maintain stable serum values and reduces this complication. Other prospective studies should be carried out to verify the results found.
Abstracts

412.3

The Performance of the Kidney Donor Profile Index in Predicting Outcomes for Brazilian Kidney Transplant Recipients of Standard Criteria Donors

Ana Paula Moraes1, Renato D Foresto1,2, Maria Amélia Hazin1,2, Blanca Cassão1,2, Helio Tedesco-Silva1,2, José Medina-Pestana1,2, Lúcio Requião-Moura1,2.
1Nephrology Division, Universidade Federal de São Paulo, São Paulo, Brazil; 2Hospital do Rim, Fundação Oswaldo Ramos, São Paulo, Brazil.

Background: The classification of the deceased donors into standard and expanded criteria is associated with several limitations, mainly because standard criteria donors (SCD) can present other characteristics associated with poor outcomes, which the binary classification has not contemplated. The Kidney Donor Risk Index and the derived Kidney Donor Profile Index (KDPI) included additional variables and are better associated with long-term outcomes. However, the KDPI has not been validated for Brazilian donors. Thus, this study aimed to evaluate the performance of the KDPI in predicting outcomes for kidney transplant recipients (KTR) of SCD in the Brazilian population for whom the index was not previously validated, as part of the efforts to validate the index for Brazilian donors.

Methods: A retrospective single-center cohort enrolled 1,943 KTR who received a kidney of SCD between 2013 and 2017 and followed up to 2018. The primary outcome was composed of death, graft loss, and 1-year graft function < 30 mL/min/1.73m2, estimated by CKD-Epi (eGFR). Spearman’s rank correlation coefficient estimated the linear association between KDPI and eGFR. Multivariable analysis for the primary outcome was performed by logistic regression, and the C-statistic evaluated the discrimination of the risk prediction model.

Results: Recipients were 48.5 years old, 59.6% female, and 44.8% white. Donors were 41.0 years old, 61.6% male, and 52.2% white. Among donors, the prevalence of hypertension and diabetes was 24.9% and 3.8%, respectively. The main causes of brain death were subarachnoid hemorrhage (47.3%) and traumatic brain injury (41.2%). The median of KDPI was 52% (32; 69), stratified as follows: 28.9% of KDPI1-35, 18.6% of KDPI36-50, 48.3% of KDPI51-85, and 4.3% of KDPI>85. The incidence of delayed graft function and acute rejection (AR) was 58.6% and 18%, respectively. One-year eGFR was 52.8 mL/min. An inverse correlation was observed between 1-year eGFR and KDPI: R= -0.36; CI95%= -0.40; -0.32; P<0.001. The frequency of primary outcome was 14.4%: 4.4% of graft loss, 2.9% of death, and 7.7% of 1-year eGFR<30. The primary outcome was associated with a longer time in dialysis before transplantation (OR for each month = 1.003; P=0.03), CMV-related events (OR=1.32; P=0.04), AR (OR=2.13; P<0.001), and the KDPI strata. Compared with KDPI1-35, the OR was 1.62 (P=0.03), 2.27 (P<0.001) and 2.21 (P=0.01) for strata 36-50, 51-85 and >85, respectively. This modeling reached a C-statistic of 0.64 (0.61-0.68), P<0.001.

Conclusion: Despite not being previously validated for Brazilian donors, the KDPI significantly correlated with 1-year graft function in kidney transplant recipients of standard criteria donors. Furthermore, although the predictive model had reached a moderate discriminative power, the KDPI was an independent predictor of primary outcome composed of death, graft loss, and eGFR < 30 within 1-year after transplantation.
Outcomes of Sodium–Glucose Cotransporter 2 Inhibitors And Glucagon-like Peptide-1 Receptor Agonists in Diabetic Kidney Transplant Recipients

Tarek Mahmoud1, Jude Yagan1, Amal Hasan2, Osama Gheith1, Mohamed Mostafa1, Suzzan Rida1, Nabil El-Serwi1, Mohamed Shaker1, Mahmoud Khalid1, Prasad Nair1, Torki Alotaibi1.
1Nephrology, Organ Transplant Center, Sabah, Kuwait; 2Clinical research, Dasman Diabetes Center, Kuwait, Kuwait.

Introduction: The impact of the new glucose lowering therapies, sodium–glucose cotransporter 2 inhibitors (SGLT2i) and Glucagon-like peptide-1 receptor agonists (GLP-1RA), on managing patients with type II diabetes mellitus is very impressive with clear evidence of improving the cardiovascular and renal outcomes. Kidney transplant recipients (KTRs) with diabetes mellitus have higher risks for cardiovascular and renal morbidities and mortalities. The use of these drugs was limited by the postulated fear of their side effects on renal graft outcomes. Few case series and small prospective trials in KTRs were published in the literature. We retrospectively assessed the safety and short-term outcomes of these drugs in our patients.

Patients and Methods: We collected data from records of 98 diabetic KTRs who received SGLT2i and another 41 who received GLP-1RA for at least 3 months. We compared them to a matched group of 70 diabetic KTRs on standard of care (SOC) therapy. Patients were at least 3 months post-transplant with stable renal function at the time of inclusion and estimated glomerular filtration rate (eGFR) of at least 25 ml/min/1.73m2. The groups were matching regarding age, gender, body mass index (BMI), type of donor, immunosuppression, post-transplant duration and type of diabetes. HbA1c was higher in both study groups compared to control (8.0% versus 7.2%). Follow up data for one year was recorded.

Results: HbA1c dropped by 0.4% in both SGLT2i (p=0.0001) and GLP-1RA (p=0.0033) groups compared to a reduction by only 0.05% in the control group. BMI decreased by 0.32 for the SGLT2i group (p=0.0450) and by 0.34 for the GLP-1RA group (p=0.0105) while increased by 0.015 for the control group. There was a tendency for better estimated glomerular filtration rate (eGFR) towards the end of the year in both study groups though it was not statistically significant except for the group of KTRs on SGLT2i with eGFR more than 90ml/min (p=0.0135). A dip in eGFR was observed in KTRs on SGLT2i at one and 3 months. Albuminuria was significantly reduced at 12 months in SGLT2i group by a median of 28 mg/mmol of creatinine (p=0.0095) and by 20 mg/mmol creatinine in GLP-1RA group (p=0.0072) compared to increase by 3.4 mg/mmol creatinine in the control group. Side effects of the drugs were minimal and comparable to the control group.

Conclusion: Use of SGLT2i and GLP-1RA is safe in diabetic kidney transplant recipients and is associated with better outcome with no increased side effects. Conducting randomized control trials is extremely required to confirm these findings and establish the guidelines.
**412.5**

**Effect of Vitamin K2-Supplementation on Calcification Propensity and Vascular Stiffness in Vitamin K-Deficient Kidney Transplant Recipients: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial**

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1Department of Internal Medicine, Division of Nephrology, University of Groningen and University Medical Center Groningen, Groningen, Netherlands; 2Department of Laboratory Medicine, University of Groningen and University Medical Center Groningen, Groningen, Netherlands; 3Department of Biochemistry, Cardiovascular Research Institute Maastricht (CARIM), University of Maastricht, Maastricht, Netherlands; 4Department of Clinical Chemistry, University Hospital Bern (Inselspital), Bern, Switzerland.

**Introduction:** Even after successful transplantation, kidney transplant recipients (KTR) remain at increased risk of vascular calcification and subsequent cardiovascular death. Vitamin K-deficiency is common among KTR, which likely contributes to increased vascular calcification. We therefore studied the effects of vitamin K-supplementation on calcification propensity, vascular stiffness and vitamin K-status in KTR.

**Methods:** Between September 2020 and July 2021, we recruited clinically stable KTR for this single-center, parallel-group, randomized, double-blind, placebo-controlled trial. Vitamin K-deficiency was the main inclusion criterion, and was defined as a previously measured dephosphorylated uncarboxylated matrix gla protein (dp-ucMGP) > 500 pmol/L. Patients using a vitamin K-antagonist were excluded. Participants were randomized 1:1 to vitamin K2 (menaquinone-7, 360 µg once daily) or placebo for 12 weeks. The primary endpoint was serum calcification propensity (calciprotein particle maturation time, T50), and the main secondary endpoint was vascular stiffness (pulse wave velocity). Further secondary endpoints included dp-ucMGP and the ratio of uncarboxylated osteocalcin over carboxylated osteocalcin (ucOC/cOC) as markers of vitamin K-status, vitamin K-uptake and biological activity of vitamin K. Treatment effects were assessed by comparing changes in primary and secondary endpoints between treatment and placebo arms using T-tests or Mann-Whitney U-tests, depending on distribution.

**Results:** Forty KTR (35% female, mean age 57 ± 13 years; median 9 [IQR: 5 to 15] years after transplantation) were randomized. The treatment groups (both N=20) were comparable at baseline. We observed no effect of vitamin K-supplementation on calcification propensity (change in T50, placebo: +0.8 ± 34.4 minutes; treatment: +2.3 ± 27.4 minutes; p=0.88), while we did observe a significant treatment effect on vascular stiffness (change in pulse wave velocity, placebo: +0.25 ± 0.43 m/s; treatment: -0.06 ± 0.26 m/s, p=0.010, Figure). Uptake and biological activity of vitamin K2 were confirmed by strong decreases in dp-ucMGP (relative change: -34% [IQR: -46% to -24%]) and ucOC/cOC ratio (relative change: -49% [IQR: -65% to -21%]) in patients in the treatment arm.

The study was supported by the Dutch Kidney Foundation (Nierstichting). The subsidizing party had no role in the design or conduction of the study, or in the writing and publication process.

**Discussion:** Although vitamin K2-supplementation did not alter calcification propensity, we observed a significant beneficial treatment effect on vascular stiffness, suggesting that vitamin K2 may have local vascular effects in the absence of detectable systemic effects on calcification propensity. These results set the stage for studies addressing long-term intervention with vitamin K2 supplementation in KTR.
Poor Sleep Quality, Fatigue, Social Participation and Healthrelated Quality of Life in Kidney Transplant Recipients


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Background: Fatigue and limited health-related quality of life (HRQoL) are common among kidney transplant recipients (KTR). We hypothesized that both may partly be attributable to poor sleep.

Methods: We used data of KTR (≥1 year after transplantation) and healthy controls (HC) from the TransplantLines Biobank and Cohort Study. Sleep quality was assessed using the validated Pittsburgh Sleep Quality Index. Determinants of poor sleep quality were identified using logistic regression. Associations of poor sleep quality with fatigue, societal participation, and HRQoL were assessed using linear regression. Among a subgroup of KTR, sleep quality was assessed before, at six and twelve months after transplantation, allowing to assess sleep quality trajectories over time.

Results: We included 872 KTR (61.1% male, age 55.7±13.1y) with available data on sleep ≥1 year after transplantation, and 335 HC. In total, 16.7% of male KTR and 31.0% of female KTR reported poor sleep quality, which was significantly higher compared to HC (males: 8.8%, P=0.017 and females: 15.5%, P<0.001). Next to female sex, more anxiety and calcineurin inhibitor usage were main determinants of poor sleep quality. Additional analyses suggested effect modification by age for the latter, and subgroup analyses confirmed that calcineurin inhibitors were associated with increased risk of poor sleep quality only in patients <57 years old (OR 6.14, 95%CI 1.87-20.15). Poor sleep quality was associated with more fatigue (st. β 0.34, P<0.001), lower ability to concentrate (st. β 0.27, P<0.001), poorer societal participation (restriction score: st. β -0.24, P<0.001), and lower HRQoL (physical component: st. β -0.32, P<0.001 and mental component: st. β -0.40, P<0.001, see Figure 2 for differences per subdomain of HRQoL) among KTR, which all remained independent of potential confounders. Longitudinal data in a subgroup of 124 participants showed that sleep quality improved after kidney transplantation in males (P<0.001), but not females (Figure 3).

Conclusion: Poor sleep quality is common among KTR. Additionally, these results highlight the clinical and personal importance of sleep quality and indicate that sleep may potentially be a key target to improve fatigue, societal participation, and HRQoL.

Astellas BV. Chiesi Pharmaceuticals BV.
412.7
Pre-transplant Hyperparathyroidism and Adverse Posttransplant Outcomes in Kidney Transplant Recipients

Fernanda Rodrigues1, Willemijn van der Plas1, Camilo Sotomayor1, Amarens van der Vaart1, Kremer Daan1, Gerjan Navis1, Stephan J L Bakker1, Martin H de Borst1, 1Department of Nephrology, University Medical Centre Groningen, Groningen, Netherlands.

Introduction: Whether correction of severe hyperparathyroidism (HPT) is required before kidney transplantation is subject of debate, as previous studies investigating the impact of pretransplant HPT on graft and patient outcomes showed conflicting results. We aimed to assess whether pretransplant serum PTH levels are associated with the risk of delayed graft function (DGF), death censored graft failure (DCGF), or mortality. Additionally, we focused on a subgroup of patients with very high pre-transplant PTH levels (>81 pmol/L; >764 pg/mL).

Methods: We performed a single-center cohort study including patients who underwent kidney transplantation between 1986 and 2020. Donor and recipient demographic data, medical information and routine laboratory measurements were extracted from the local transplant registry. We performed multivariable logistic regression and Cox regression analyses to study associations between PTH and DGF (persisting dialysis requirement for up to 7 days post-transplant), DCGF (return to dialysis or re-transplantation), or all-cause mortality, respectively. We also compared these outcomes for patients in the highest vs. lowest PTH decile for each endpoint.

Results: A total of 1576 kidney transplant recipients (KTRs) (51.6 ± 14.0 years-old, 42.7% male) were included. Donor age was 51.2 ± 13.5 years, 785 (49.8%) patients received a graft from a living donor, and 535 (33.9%) patients underwent a pre-emptive transplantation. Median (IQR) pretransplant serum PTH concentration was 24.3 (12.8 – 44.8) pmol/L. Corrected calcium increased while PTH and corrected phosphate decreased within the first 3 months post-transplant, even in patients with pre-transplant PTH >81 pmol/L (Figure 1A-C). Pre-transplant PTH was not associated with DGF (Table 1). During median follow-up of 5.0 (2.2 – 8.4) years, 201 (12.8%) patients developed DCGF. In fully adjusted Cox regression analyses, PTH was not associated with DCGF (Table 1). Additionally, patients with PTH >81 pmol/L (N=121) did not have an increased risk of DGF (HR 1.67 [95% CI 0.62 – 4.48], P=0.65). In the highest vs. lowest PTH decile for each endpoint, there was also no association with mortality (HR 0.96 [95% CI 0.62 – 1.48], P=0.65).

Conclusion: In this cohort study, pre-transplant serum PTH was not associated with an increased risk of DGF, DCGF or mortality after transplantation. Subgroup analyses in patients with severe HPT yielded similar results. Our data compared to previous studies. Additionally, we also assessed the outcomes for patients in the highest vs. lowest PTH decile for each endpoint. We found no association between PTH and DGF or mortality in the highest decile. However, in the lowest decile, we observed a trend towards increased risk of mortality, which was not statistically significant. These findings support the current practice of not performing pre-transplant parathyroidectomy in patients with severe hyperparathyroidism.

412.8
Proton-Pump Inhibitor Use, Fatigue and Health-Related Quality of Life in Kidney Transplant Recipients

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Background: The role of the gut-brain interaction in fatigue etiology and health-related quality of life (HRQoL) has become increasingly clear in the past decades. Recently, it has been shown that the gut microbiota can be affected by the use of proton-pump inhibitors (PPIs). Given the common use of PPIs among kidney transplant recipients (KTR), we hypothesized that PPI use may be an important and underappreciated determinant of fatigue and HRQoL in this population.

Methods: Data of KTR (>1 year after transplantation) from the TransplantLines Biobank and Cohort Study were used. PPI use was retrieved from medical records and verified with study participants. Severe fatigue and HRQoL were assessed using the validated CIS20R and SF-36 questionnaires.

Results: A total of 937 KTR (39% male, mean age 56±13 years) were included at a median of 3 [1-10] years after transplantation. PPIs were used by 656 (70%) KTR. Severe fatigue was more prevalent among PPI users compared to non-PPI users (36% vs. 22%, p<0.001). In addition, both physical and mental HRQoL scores were lower among PPI users compared to non-PPI users (physical: 67 ± 22 vs. 75 ± 19, p<0.001; mental: 75 ± 18 vs. 79 ± 17, p<0.001). In regression analyses, PPI use was independently associated with a higher risk of severe fatigue (OR 2.25, 95%CI 1.53 to 3.30, p<0.001), lower physical HRQoL (B -6.42, 95%CI -9.48 to -3.36, p<0.001) and lower mental HRQoL (B -4.10, 95%CI -7.67 to -1.43, p=0.003). Additional analyses showed that these associations were dose-dependent, present among all individually assessed PPI types and dependent on duration of PPI use. These associations were dose-dependent, consistent for all individually assessed PPI types and dependent on duration of PPI use. We also compared these outcomes for patients in the highest vs. lowest PTH decile for each endpoint. We found no association between PTH and DGF or mortality in the highest decile. However, in the lowest decile, we observed a trend towards increased risk of mortality, which was not statistically significant. These findings support the current practice of not performing pre-transplant parathyroidectomy in patients with severe hyperparathyroidism.

Conclusion: In this cohort study, pre-transplant serum PTH was not associated with an increased risk of DGF, DCGF or mortality after transplantation. Subgroup analyses in patients with severe HPT yielded similar results. Our data compared to previous studies. Additionally, we also assessed the outcomes for patients in the highest vs. lowest PTH decile for each endpoint. We found no association between PTH and DGF or mortality in the highest decile. However, in the lowest decile, we observed a trend towards increased risk of mortality, which was not statistically significant. These findings support the current practice of not performing pre-transplant parathyroidectomy in patients with severe hyperparathyroidism.

Association of PPI use with severe fatigue and health-related quality of life

Logistic regression with severe fatigue as dependent variable

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Linear regression with health-related quality of life as dependent variable

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<td>Creatinine</td>
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<td>&lt;0.001</td>
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Patient characteristics: age, sex, body mass index, blood pressure, diabetes, prior cardiovascular disease, current use of blood pressure medication, cholesterol, triglycerides, smoking status, alcohol use, PPI use, depressive symptoms, anxiety, depression, social support, physical activity, self-esteem, global health status, health-related quality of life, and all-cause mortality. Abbreviations: B, beta; CI, confidence interval; OR, odds ratio; PPI, proton pump inhibitor.
Association of Skin Cancer with the Use of Azathioprine and Mycophenolate Mofetil in Kidney Transplant Recipients

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Introduction: Skin cancer, especially squamous cell carcinoma (SCC), is the most common type of cancer among kidney transplant recipients. SCC is more likely to spread (metastatic SCC), which can result in the patient’s death. The cause of skin cancer among transplant patients is thought to be due to immunosuppressive therapy. These drugs must be used for a long time to prevent organ rejection, but they limit the immune system’s ability to destroy UV-damaged cells, allowing these damaged cells to grow into malignancies. In transplant patients, ultraviolet (UV) exposure is a crucial contributor to the development of skin cancer. Our study aims to assess the association of skin cancer with the use of Azathioprine and Mycophenolate Mofetil in kidney transplant recipients.

Methodology: Data of 941 patients who had renal transplantation between 1998 and 2018 in University Hospitals of Coventry and Warwickshire were retrospectively reviewed. Data contained information about age, gender, ethnicity, type of transplant, the previous number of transplantation, cancer status, medication, dose, duration of medication, skin cancer diagnosis results, non-skin cancer diagnosis results, treatment start date, treatment follow-up with a time gap of 6 months, 1, 5, 10, 15 and 20 years, and type of treatment they had. Exclusion criteria: HLA incompatible transplant, patients with pre-transplant skin cancer, patients with incomplete data, and patients who switched from azathioprine to Mycophenolate Mofetil or vice versa. Cox proportional hazard regression analysis was used to evaluate factors associated with a higher risk of skin cancer. Analysis of variance (ANOVA) test was used to compare the relationship between Azathioprine versus Mycophenolate Mofetil and subtypes of skin cancer.

Results: Overall, there was no significant difference between Azathioprine and Mycophenolate Mofetil in terms of occurrence of skin cancer (HR=1.05, P=0.87, 95%CI: 0.56-1.94). An increase in the number of previous transplants was associated with a higher risk of skin cancer (HR=2.48, P<0.01, 95%CI: 1.23-5.01). Patients with age>50 years old were associated with a higher risk of skin cancer (HR=4.98, P<0.01). On further subgroup analysis using ANOVA, Mycophenolate Mofetil was associated with a higher risk of developing basal cell carcinoma (BCC) (52.6%) in comparison to Azathioprine (22.6%) with a P value<0.05. Azathioprine was associated with a higher risk of developing squamous cell carcinoma (25.8%) in comparison to Mycophenolate Mofetil (15.8%) with P value<0.05.

Conclusion: There was no significant difference between Mycophenolate Mofetil and Azathioprine in terms of occurrence of skin cancer. Increase in age, and the number of the previous transplant are associated with a higher risk of skin cancer. Azathioprine is associated with a higher risk of developing SCC while Mycophenolate Mofetil is associated with a higher risk of developing BCC.
Blocking of the CD40-CD154 Pathway Inhibits Macrophage Infiltration and Reduces Fibrosis After Renal Transplantation

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Introduction: Renal transplantation improves the life expectancy and quality of life of end-stage renal patients. Due to the development of immunosuppressive drugs, the results of short-term renal transplantation have improved significantly, but the long-term survival rate of renal transplantation has hardly changed in the past few decades. Interstitial fibrosis is an important cause of graft loss in chronic allograft renal injury. CD40-CD154 costimulatory pathway block can inhibit T cell activation and prolong the survival of allografts in a variety of transplantation models. In this study, we found that the single use of MR1 (CD154 antibody) can significantly reduce the fibrosis of transplanted kidney.

Method: The kidney of BALB/c mice was transplanted into C57BL6/J recipient by orthotopic transplantation. The contralateral kidney of the recipient was removed 1-3 days after transplantation. The MR1 treatment group was intraperitoneally injected with 500μg of MR1 antibody on the day of operation, and the control group was given normal saline at the same time. After 30 days, serum was collected to measure the blood creatinine. The kidney was obtained after cardiac perfusion. PAS staining was used to detect renal injury. The number of T lymphocytes and macrophages and the expression of α-SMA in the transplanted kidney were analyzed by flow cytometry. Sirius red and gomori trichrome staining were used to detect fibrosis. The colocalization of macrophages and α-SMA was detected by multiple immunofluorescence.

Results: It was found that serum creatinine from MR1 treatment group was significantly lower than control group. Compared with control group, MR1 treated mice also showed milder renal histological lesions that the loss of brush border of proximal tubules, tubular necrosis, tubular atrophy, protein casting and cell infiltration at the cortical medullary junction were much lower. Sirius red and gomori trichrome staining showed that the number of macrophages and the expression of α-SMA in the transplanted kidney were significantly reduced compared to control group. Through flow cytometry analysis, it was found that the number of macrophages secreting α-SMA in control group were significantly higher than those in MR1 treatment group. The FACS results showed that 92.7% ± 2.8% of the infiltrating macrophages were M2 type, and they were all derived from the recipients. Immunofluorescence experiment also confirmed this result.

Conclusion: MR1 significantly reduced the fibrosis in kidney graft which may due to less infiltration of M2 macrophages and less α-SMA+ macrophages.

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New-Onset Osteoporotic Fracture After Kidney Transplantation: A Matched Comparative Nationwide Cohort Study

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Background: Successful kidney transplantation (KT) has brought better survival and quality of life to patients with end-stage kidney disease (ESKD), although long-term immunosuppressive agent-related side effects such as osteoporosis remain unresolved. We aim to explore the incidence risk of de novo osteoporotic fractures after KT compared with matched dialysis patients.

Method: We constructed a nation-wide retrospective cohort consist of 141,674 ESKD patients from 2008 to 2020 using the National Health Insurance System database of Korea. After 1-year of wash out periods, patients younger than 18-year-old, having previous history of any kind of cancer, experiencing parathyroidectomy, re-transplantation, osteoporotic fracture, or taking osteoporosis-treating medication were excluded. Then, we extracted KT recipients and 1:1-matched dialysis patients according to the age, sex, era, and the presence of hypertension or diabetes. Osteoporotic fractures are defined as fractures associated with low bone mineral density including hip, spine, forearm, and humerus. We compared the de novo osteoporotic fracture incidence between the two groups.

Result: After exclusion of 26883 patients in wash-out periods, 483 children, 6953 having cancers, 336 experiencing parathyroidectomy, 8907 preexisting osteoporotic fractures, 3755 established osteoporosis medications, and 110 re-transplantations, we finally identified 12760 matched KT-dialysis pairs. Their average age was 51.0 ± (10.1) (standard deviation (SD)) years and 7951 (62.3%) were male. Patients with having hypertension or diabetes were 11800 (92.5%) and 4548 (35.6%), respectively. About 30.5% KT patients received their graft preemptively. New-onset osteoporotic fractures after inclusion occurred in 631 (4.9%) of dialysis patients and 588 (4.6%) of KT recipients, respectively. The most common fracture site was forearm in both groups. During overall 4.7 ± 3.1 years of follow up, KT recipients showed similar risk for the development of new-onset osteoporotic fracture compared with matched dialysis controls even after adjustment of matching variables, previous use of steroid or anti-depressants, vitamin D or its analog, calcium-based phosphate binders. In subgroup analysis, they showed a lower risk of hip fracture (adjusted hazard ratio 0.51, 95% CI 0.38-0.67, p <0.001), but similar risks of other types of osteoporotic fractures including spine, forearm, or humerus compared to dialysis controls.

Conclusion: In this study, overall new-onset osteoporotic fracture risk of KT recipients was not different from matched dialysis controls except a lower risk of hip fractures.
Post-transplant Lymphoproliferative Disorders After Solid Organ and Hematopoietic Stem Cell Transplantation: A Nationwide Cohort Study in Korea

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Introduction: Post-transplant lymphoproliferative disorders (PTLD) are the majority of cancer diagnoses after solid organ transplantation (SOT) and allogeneic hematopoietic stem cell transplantation (HSCT) with a high incidence of PTLD developed in the first post-transplant year. However, there is minimal nationwide literature examining the incidence and risk analysis of PTLD. We investigated the incidence and risk determinants of PTLD in Korean SOT and HSCT recipients using a large national database.

Method: This study recruited 47,708 patients (SOT: 37,023; HSCT: 10,685) from the Korean National Health Insurance Service database between 1 January 2009 and 31 December 2020. Patients previously diagnosed with hematologic or lymphoproliferative malignancies or multi-organ transplant recipients were excluded.

Results: PTLD developed in 432 patients (SOT: 257; HSCT: 175). According to the type of transplant, PTLD after HSCT was the most common (1.64%), followed by heart (1.16%), lung (0.98%), liver (0.83%), kidney (0.57%). The subdistributional hazard ratio (SHR) of PTLD in pediatric patients younger than 9 years of age was higher than that in those aged 20 to 39 years (SHR: 2.184, p < 0.001, 95% confidence interval [CI]: 1.490-3.201). When compared with SOT, HSCT was associated with a greater risk of PTLD (SHR: 1.833, p < 0.001, 95% CI: 1.461-2.299). The hazard ratio (HR) of death after diagnosing PTLD in patients aged over 60 years was higher than that in those aged 20 to 39 years (HR: 2.612, p < 0.001, 95% CI: 2.411-2.830). When compared with SOT, HSCT was associated with a greater risk of death after PTLD (HR 5.075, p < 0.001, 95% CI: 4.829-5.332).

Conclusion: This nationwide population-based cohort study revealed that PTLD was associated with a higher risk of pediatric age, especially in the 0-9 years age group. According to the type of transplantation, HSCT was at greater risk of developing PTLD and death after the diagnosis of PTLD than SOT.
413.1
The Impact of UNOS Acuity Circles-Based Organ Allocation on DCD Liver Transplant Rates and Waitlist Mortality in the United States

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Background/ Aim: The acuity circles -based liver allocation policy (AC) has aimed to shift ideal donor livers from “lower MELD” to “higher MELD” regions, which could have variable geographic effects on waitlist outcomes and organ acceptance of marginal allografts, such as those from donors after circulatory death (DCD). We aimed to explore how AC affected DCD liver transplantation (LT) and waitlist mortality (WLM) across the United States.

Method: Study period: 01/2016-08/2021. Waitlist and transplant datasets were retrieved from the Scientific Registry of Transplant Recipients. All adult DCD LTs were included. The cohort was dichotomized into pre-AC (01/2016-02/2020) and post-AC eras (02/2020-08/2021). Annual state-based DCD LT rates were calculated as a function of waitlist size (the number of DCD LTs/ waitlisted patients/year), and waitlist mortality (WLM) was calculated as the number of waitlist removals due to death over the number of patients on the waitlist per State/year. State-based differences (Δ) in DCD rate (ACD) and WLM rate (AWLM) were measured pre- and post-AC.

Results: AC implementation coincided with an increase in the overall LT activity (average 8229 LT/year pre-AC vs. 8873 in 2020), and overall DCD LT (average 552 DCD LT/year pre-AC vs. 830 in 2020). Following implementation of the new allocation policy (table 1):

- Overall waitlist mortality remained unchanged (9%, range -10 to 13%).
- Overall DCD transplant rate shifted from 6% to 8% (NS), with tremendous variation among States (ACD rate -1% to +14%). The sharpest increase was noted in Arizona (14%), followed by Louisiana (5%), Arizona (4%), and Mississippi (4%).
- The highest absolute DCD rate was met in Arkansas (36%), followed by Arizona (31%), with respective AWLM of -3% and 0%.
- Southern States had a median increase of their DCD rates (ACD) 2 (IQR 1, 4; range 14) with a median increase of their WLM by 0.5% (IQR -0.5%, 2%);
- Coastal States had a median ACD of 1 (IQR 0.1, range 3) with a median increase of their WLM by 1.5% (IQR -1%, 3.5%).

Conclusion: The pre-AC era was associated with no significant differences in WLM overall but varied tremendously across states. State-based differences in DCD LT were notable post-AC, particularly in the South and Southwest. This study suggests that the AC policy has had geographically variable impact on waitlist outcomes and DCD LT use. Better understanding of center practices and outcomes in the post-AC era is critical to evaluate the impact of organ allocation policy changes on stakeholders.

413.2
Donation After Cardiac Death (DCD) Liver Grafts From Elderly Donors: A Comparative Analysis of Feasibility and Outcome

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Introduction: Advanced donor age is a known factor to affect the post-operative functional outcome of deceased donor liver transplantation (DDLT) and is in fact the biggest attributable factor to high donor risk index (DRI). When paired with donation after cardiac death (DCD), the risk of transplantation increases several folds thereby precluding the use of such grafts at most centres worldwide. With a high threshold of rejecting such grafts at our centre, we aim to analyse the outcomes of liver transplantation using elderly DCD grafts and assess its feasibility.

Methods: All patients having undergone DDLT between January 2016 and December 2021 were included in the study. The population was divided into 4 groups: DCD grafts (<50 years and >50 years) and DBD (Donation after brain death) grafts (<50 years and >50 years). The peri-operative and post-operative outcomes were compared. The borderline grafts having placed on Organox machine perfusion for optimisation were excluded from the study (n=9).

Results: Of the 807 patients included in the analysis, 88 (10.9%) received a graft from the DCD donors including MAiD (Medically assistance in dying) donors, with 38 (43%) of them being from the elderly donors. In the DBD group (n=719; 89%), 323 (45%) received grafts from the elderly donors. The demographic and peri-operative parameters were comparable in both groups (Figure 1).

The overall incidence of post-operative biliary stricture was higher for the DCD grafts compared to DBD (13%; 14.7% vs 31%; 4.3%; p=0.001). However, the same was slightly lower in the elderly DCD group (n=3; 7.8%) compared to the younger group (n=10; 20%); p=0.11, with a higher occurrence of anastomotic stricture in the elderly group (n=2; 67%) and non-anastomotic in the younger group (n=9; 90%); p=0.1 (Figure 1). There was no significant difference between the mortality of the younger vs elderly groups in DCD (14% vs 13%; p=0.9) and DBD (10% vs 6%; p=0.08) cohorts. The 1-, 3- and 5-year survival of the DCD grafts (94%, 88%, 72%) were comparable to that of the DBD grafts (96%, 87%, 62%); p=0.09. Also, the patients receiving elderly DCD grafts showed similar graft survival rates compared to the younger DCD grafts (90%, 80%, 68% vs 91%, 81%, 65%; p=0.56). There was no significant difference in the 1-,3- and 5- year survival rates of patients among the 4 groups (Figure 2).

Conclusion: Donor age alone should not be the criteria to decide the acceptability of DCD grafts in liver transplantation. With proper selection criteria, elderly DCD grafts could be a valuable contributor to expand the liver donor pool with comparable results to lesser damaged younger DDBD grafts.

Survival proportions: Survival of DCD vs NDD survival

![Survival proportions: Survival of DCD vs NDD survival](image-url)
Towards a National System of Living Donor Follow-up in Canada

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Introduction:
Despite the provision of universal health care, there are several real or potential gaps in the post-donation care of living kidney donors in Canada. Health services are administrated by provincial governments and there is no national standard for living donor follow-up. In the absence of a national standard, transplant programs lack dedicated funding to ensure appropriate long-term follow-up of living donors and there is no mechanism to obtain national information about the health outcomes of living donors including death or kidney failure.

Methods:
We describe our ongoing work-plan to establish national consensus on the follow-up of living kidney donors in Canada and to establish funding for a new national system of living donor follow-up. This work was financially supported by Canadian Blood Services. The results of completed activities will be presented.

Results:
The work-plan includes: 1) An environmental scan of the current practice of living donor follow-up. This showed significant clinical practice variation between the 28 adult and pediatric kidney transplant programs. 2) A literature search to determine international models of living donor follow-up, which revealed significant international variation in practice and failed to identify a preferred model for implementation in Canada. 3) A survey of 685 living donors, which was undertaken to determine donors’ experience, needs, satisfaction and preferences for follow-up. The survey revealed that most (72%) of donors receive follow-up from a primary care physician, a minority (30%) of donors were dissatisfied with their follow-up, and two thirds endorsed life-long follow-up after donation. 4) A stakeholder conference including past donors, transplant professionals and researchers will be held in October 2022. This conference will include presentation of background information, breakout discussions led by facilitators and a plenary session in order to establish consensus recommendations on living donor follow-up including donor consent, essential data capture, and implementation recommendations. The workshop recommendations will also be used to produce a report. Finally, we plan to advance a business plan to implementation in all 28 kidney transplant programs.

Conclusions:
The presentation will summarize our workplan and findings to date. The information may be useful in other countries or regions considering establishment of living donor follow-up programs.

This work was financially supported by Canadian Blood Services.

Figure 1: Comparison of demographic and peri-operative variables among the 4 groups
The Beginning of the End for Living Unrelated Donation Kidney Transplantation in the Middle East: The Shiraz Transplant Center Experience

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Background: The Middle East is a region with much controversy and limitations regarding deceased organ transplantations. In this report we describe our unique experience with the establishment of our deceased donor organ donation program for Central and Southern Iran.

Methods: During the initial phases in the 70s and 80s, only living related kidney transplantations were allowed in Iran. However, this policy was not continued and was expanded due to severe shortage of hemodialysis facilities and an urgent need to increase the number of kidney transplantations. Accordingly, some centers in Tehran started unrelated kidney transplantation with the support of the government that offered bonuses to persuade unrelated donors. It should be mentioned that, during this time, permission for deceased organ donation was not yet obtained in Iran. The main focus of the Shiraz Transplant Center was to develop a deceased donation program from the beginning. During three decades this center was able to expand its deceased donation program to a degree that in 2008 it completely replaced all its unrelated kidney donations by deceased donations. Prior to 2008, most transplantations were related living and deceased donations, and only in cases where a patient was on the wait list for more than one year and a compatible donor was not found, they were only allowed to have living unrelated donations. The deceased program in the STC has since expanded and has aimed to stop unrelated living donations to achieve some goals which include: to abide by ethical guidelines in organ donations/transplantation such as the declaration of Istanbul, and to finally change the dominant practice of unrelated living donations within the Middle East. These efforts have resulted in an increase of deceased donations in Iran from 1.6 in 2004 to 14.34 per million population in 2019, and in some areas this has reached to as high as 50.

Results: Up to March 2021, in the STC, overall 5389 kidney transplantations have been performed. Figure 1 shows the trend in kidney transplantation in the STC.

Conclusion: Living unrelated donations are still an ongoing issue in the Middle East region. Our center, has implemented a wide deceased donor program and as a result has been able to completely stop unrelated living kidney transplantations. The deceased donor organ donation program should further be expanded within Iran and other countries in the region and continuous campaigns should be held up against any type of unethical issues such as living unrelated transplantations to meet with international standards.

HCV-Viremic Donor Allograft Consideration by Organ Type And Year, Among Adult and Pediatric Solid Organ Transplant Candidates

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Introduction: Use of HCV-viremic donor organs (D+) for transplant into HCV-seronegative recipients (R-) has been shown to be safe and equally effective as using HCV-seronegative donor organs since 2016. Therefore, we sought to evaluate changes in frequency of transplant candidates being listed as willing to consider offers of HCV-viremic donor organs (“HCV offer interest”) from 2015-2021 as a measure of greater openness to HCV D+R-transplants among transplant candidates and centers.

Methods: We identified all waitlist candidates 2015-2021 listed for kidney, liver, heart, or lung transplantation in the United States using the Scientific Registry of Transplant Recipients. Waitlist candidate HCV serostatus was not available, but permission for waitlist additions for HCV-related disease in the United States is declining. We compared patient and center characteristics using Chi-square and McNemar tests, by HCV offer interest, for pediatric (<18 years old) and adult transplant candidates.

Results: We identified 392,515 waitlist candidates (269,770 kidney, 69,728 liver, 32,418 heart, 20,599 lung), including 377,375 adult and 15,140 pediatric candidates. Overall, 33.8% of adult and 4.1% of pediatric candidates were recorded as interested in HCV D+ organ offers (<0.001, Table 1). HCV offer interest varied by organ type among both adult (30.3% kidney vs. 42.3% liver vs. 45.0% heart vs. 35.3% lung, p<0.001) and pediatric candidates (2.0% kidney vs. 3.0% liver vs. 7.3% heart vs. 12.9% lung, p<0.001). All organ types showed increased HCV offer interest over time (Figure 2). The percentage of transplant centers who had at least one pediatric candidate listed as interested in HCV D+ offers had a trend toward an increased from 2015 to 2021 for kidney (4.5% vs. 12.1%, p=0.07), liver (3.6% vs. 9.4%, p=0.06), heart (7.1% vs. 16.1%, p=0.1), and lung candidates (12.0% vs. 33.3%, p=0.5). The percentage of transplant centers who had at least one adult candidate listed as interested in HCV D+ organ offers remained stable from 2015 to 2021 for kidney (74.2% vs. 77.4%, p=0.8) and liver (92.4% vs. 93.4%, p=0.4) candidates and increased for heart (48.6% vs. 72.1%, p<0.001) and lung (31.8% vs. 58.9%, p<0.001) candidates.

Conclusion: Willingness to consider HCV-viremic donor organs has increased since 2015 at the patient and center levels among pediatric and adult candidates, especially pediatric lung transplant candidates. This reflects the increasing recognition of the safety and efficacy of HCV-viremic organ transplants into HCV-seronegative recipients. However, a substantial percentage of transplant centers still have no candidates listed as willing to consider HCV-viremic donor offers, possibly indicating a lack of comfort with HCV D+R-transplants. We must address this discomfort with educational initiatives to ensure this valuable organ pool is available to as many waitlist candidates as possible.

Table 1. Characteristics of (A) Pediatric and (B) Adult Kidney, Liver, Heart, and Lung Transplant Candidates, by Willingness to Consider HCV-Viremic Donor Organ Offers

<table>
<thead>
<tr>
<th>Organ Type</th>
<th>Kidney</th>
<th>Liver</th>
<th>Heart</th>
<th>Lung</th>
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<td>No</td>
</tr>
<tr>
<td>Age (years)</td>
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<td>0-17</td>
<td>18-64</td>
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<tr>
<td>Sex</td>
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<td>Female</td>
<td>Male</td>
<td>Female</td>
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<td>White</td>
<td>Black</td>
</tr>
<tr>
<td>HCV Status</td>
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<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Offer Interest</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Note: All comparisons were made using Chi-square and McNemar tests, by HCV offer interest, for pediatric (<18 years old) and adult transplant candidates.
How Whole Slide Imaging and AI Can Improve Organ Transplants

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Introduction: As the advancement and implementation of technology in healthcare diagnostics continue, the full capabilities may not be fully realized. Research and development of artificial intelligence (AI) within the transplantation realm are primary examples. The expansion of whole slide imaging and AI in kidney and liver transplantation presents immense opportunities to address significant logistical concerns. This includes the quality of pathology reports, speed of organ offer acceptance, and minimizing ischemic time. Globally, there is a high demand for organs to compensate for the increasing diagnosis of comorbidities requiring transplantation. Unfortunately, the technical and logistical barriers of evaluating cadaveric donor organs in an emergent but precise manner prohibit efficient allocation. Organ allocation can be further refined and post-transplant outcomes improved by seeking solutions that will produce consistent, high-quality pathology reports, regardless of time or properly trained pathologists. The implementation of AI stands to address these issues by introducing machine learning in accurately reading donation biopsies.

Methods: In the case of kidney and liver transplantation, when a cadaveric donor becomes available, biopsies are acquired to assess the viability of organ transplantation. Under ideal circumstances, these biopsies are read by a specialized pathologist. But many times biopsies are read by any available pathologist. This results in sub-par, inconsistent, and frequently delayed pathology reports. The reliance upon these reports subject’s organ recipients to inconsistent results that will impact long-term outcomes. Once the slides are digitized an AI algorithm can be trained to provide a consistent, accurate organ donation-focused pathology report at any time of day.

Conclusion: Whole slide imaging and AI can fill the gaps that negatively impact surgical decision-making and long-term patient outcomes. Technology that can improve the quality and accuracy of pre-transplantation biopsy reports, AI can significantly reduce the duration of getting organs to patients and avoid the transplantation of unviable organs. It can identify fibrosis and inflammation of the liver and kidney, sclerotic glomeruli, atrophied tubules in kidney samples, and large and small droplet macrosteatosis fat in liver samples. Increased efforts and resources to bolster the research and development of AI systems in transplantation can significantly benefit all parties involved in delivering high-quality care and positive long-term patient outcomes.
Abstracts

Abstract 413.7

Normothermic Machine Perfusion Compared With Static Cold Storage of Liver Grafts for Late Liver Retransplantation: Results of the NAPLES Initiative

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Introduction: The pool of donor organs available for patients undergoing liver retransplantation is small, due to the perceived need for an optimal graft. Strategies that can facilitate transplantation of suboptimal organs into retransplant candidates requires investigation. The aim of this study was to determine if patients undergoing liver retransplantation, can be safely transplanted with sub-optimal grafts following normothermic machine perfusion.

Methods: Between November 2018 and November 2021, a prospectively enrolled group of retransplant candidates consented to receive livers with suboptimal features but preserved and viability tested with normothermic machine perfusion (NMP). Donor, graft and clinical outcomes were compared to a retrospective group that underwent retransplantation with a graft preserved via static cold storage (SCS) between January 2015 and November 2021. All recipients received grafts from deceased brain death donors. The primary outcome of this study was 6-month graft and patient survival.

Results: During the study period, 37 patients underwent retransplantation with a NMP preserved graft. Three of these received two NMP preserved grafts. The CS control group comprised 54 patients, and two of these patients received two CS grafts. Therefore, the NMP and CS groups comprised 40 and 56 grafts respectively. Donor, graft, operative and outcome variables are displayed in table 1. The 6-month graft (90% v 86%, P=0.59) and patient (94% vs 93%, P=0.79) survival did not differ between groups (Table 1). This was despite the NMP group having significantly more steatotic grafts (Moderate steatosis; 30% vs 4%, P=<0.01), donors with transaminases >1000 IU/L (0% v 23%, P=<0.01), and grafts previously declined by at least one other transplant centre (78% v 26%, P=<0.01) (Table 1). The peak alanine transaminase in the initial post-operative 7 days was significantly lower (521 vs 796, P=0.02) in the NMP group, however the rate of early acute rejection was higher (50% vs 27%, P=0.02) but did not impact graft survival. Significantly higher rates of CVVH in the NMP group did not translate to a longer length of stay in ICU. Furthermore, longer term graft and patient survival did not differ between groups (Figure 1).

Conclusion: This is the first study to demonstrate that NMP technology can be safely used for sub-optimal liver grafts, and these can be safely transplanted into patients that require retransplantation. This technology can therefore expand the graft options available to this high-risk group.

Anne Fox Foundation, University Hospitals Birmingham Charity.
Controlled Asystole Donation in Patients Older Than 70 Years Old—It Is Really Worth It?

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1Intensive care unit, Hospital Virgen de la Arrixaca, Murcia-Churra, Spain.

Introduction: Organ transplantation improves the quality of life and increases the life expectancy of patients with end-stage organ failure. The demand of organs for transplant is continually increasing given the aging population, an increase in the prevalence of kidney failure, and advances in intensive care units. In Spain, more than a decade ago, controlled asystole donation (CAD) emerged as a strategy to solve the shortage of organs available for transplant. Although there is not an established age limit in controlled asystole donors, there exists an “unconscious bias” to reject asystole organs by age criteria, without doing a global valuation of the same donors. The main objective of this study is to determine if CAD in patients over 70 years of age is feasible in terms of the effectiveness of the donation and number of organs per real and used donor.

Methods: Retrospective observational study including donors in controlled asystole older than 70 years from November 2014 to September 2021 in a tertiary care hospital.

Results: During the study period, a total of 51 real controlled asystole donors were collected. Of the sample studied, the median age was 74 years, being mostly men (60.1%). Regarding cardiovascular risk factors, 62.7% patients suffered from arterial hypertension, 23.5% from diabetes, 19.6% from dyslipidemia. The most frequent blood type included was 0+ (47.1%) followed by A+ (39.2%), B+ (11.7%) and 0- (2%). The average length of stay in the critical care unit before donation was 7.6 days. The analysis of the data showed an effectiveness of 88.2%, 45 donors used out of the total number of patients included. A total of 37 livers and 40 kidneys were valid and transplanted in their appropriate receptors. In 47.1% of the total of sample it was possible to use one organ, in 19.6% two organs and in 21.6% three organs, assuming a rate of 1.51 organs per real donor and 1.71 in used donor.

Conclusion: The effectiveness of the CAD in this age group is high (88.2%), slightly above the Spanish average in 2020 (87%). Although the rate of organs per donor is low, it exceeds 1.5 organs by transplanted donor. That, in our opinion, is enough to not dismiss a potential controlled asystole donor based solely on age criteria.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Real donors (n=51)</th>
<th>Used donors (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>74 (70-78)</td>
<td>73 (70-78)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male: 52.9%</td>
<td>Male: 52.2%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23.5%</td>
<td>22.2%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>19.6%</td>
<td>19.6%</td>
</tr>
<tr>
<td>Blood group</td>
<td>0+ (47.1%)</td>
<td>A+ (39.2%)</td>
</tr>
</tbody>
</table>

Legend: Categorical variables compared with Chi-square test. Independent samples T-Test was used to compare continuous variables that followed the normal distribution. The Mann-Whitney U test was used to compare continuous variables that did not follow the normal distribution. DRI = Donor Risk Index, DLI = Donor Liver Index, UKELD = United Kingdom model for end-stage liver disease, MELD = Model for end-stage liver disease, PNF = Primary non-function, EAD = Early allograft dysfunction, ALT = Alanine aminotransferase, INR = International normalised ratio, EUC = Emergency care unit, ECMO = Extracorporeal membrane oxygenation, CVVH = Continuous veno-venous haemofiltration, COVID-19 = Coronavirus associated disease. "Reas" related to donor or graft quality, decline due to use or error diagnosis not included. Patients who received more than 1 retransplant only considered once in survival analysis based on first graft received. 30/40 grafts in the NMP have attained 6 month follow-up. During post-op hospital stay.

![Graph 1](image1)

![Graph 2](image2)

Legend: Graft and patient survival for each group. ECD=Extended cold storage, MPM=Normothermic machine perfusion.
Organ Donation Following Medical Assistance in Dying: A Scoping Review

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Introduction: While more countries are legalizing Medical Assistance in Dying (MAiD), only Canada, Belgium and The Netherlands allow for controlled organ donation following MAiD. Recently, the MAiD legislation in Canada was amended with Bill C-7, which changed the eligibility criteria for MAiD, including safeguards, potential to waive the requirement for final consent at time of MAiD procedure for reasonable natural foreseeable death, and expanding reporting requirements of MAiD procedures. To support updates in the practice guidelines and to ensure safety and ethically acceptable procedures for organ donation following MAiD, we investigated the current literature worldwide on the existing processes, procedures and outcomes regarding organ donation following MAiD.

Method: Scoping review using JBI methodology. Published and unpublished literature of any design were considered if they discussed organ donation following MAiD at home or in any healthcare setting in any country. Databases included Ovid MEDLINE, Ovid Embase, CINAHL via EBSCOhost, Ovid PsycINFO, Web of Science – Science Citation Index and Social Science Citation Index via Clarivate, and Academic Search Complete via EBSCOhost. Gray and unpublished literature included materials from organ donation organizations in Canada, Belgium and The Netherlands. Articles were screened and data extracted and analyzed using a content analysis approach by two independent reviewers. Evidence was collated using a descriptive numerical summary and a narrative content analysis approach.

Results: 1879 reports were identified and 121 were included. The reports were in English (n=95), Dutch (n=17) and French (n=9); majority from Canada (n=51), The Netherlands (n=38), and Belgium (n=14), published between 2019-2021 (n=57). Our content analysis identified several major theme areas: main processes and procedures involved in organ donation after MAiD in the hospital and at home; main clinical pathways involved in different settings; ethical dilemmas involved in this combined procedure; healthcare professionals’ roles and perceptions; impacts on organ donation and transplantation system; transplant outcomes; public perceptions; process and tools in place; educational strategies for healthcare professionals involved; and suggestions for future research to address knowledge gaps.

Conclusion: The results of this review provide important directions for improvements in the current Canadian organ donation system. These findings can also be used as a rich source of information for countries establishing organ donation following MAiD.
The Improvement Study: Call for a New International Prospective Non-competitive, Observational Study to Validate And Optimize Kinetic Models to Predict Liver Allograft Failure At 3 and 12 Months After Liver Transplantation

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Background: Allograft failure (AF) at 90 days after LT has been recently predicted by externally validated kinetic models based on graft performance during early post-operative days (North American L-GrAFT score, European EASE score), which identify patients at high risk of AF who benefit from early retransplantation (C-statistic >85%). However, with increasing utilization of ECD or DCD allografts, a higher incidence of ischemic cholangiopathy has been reported at 12 months, which is not captured when evaluating short-term outcomes. Furthermore, other factors not routinely evaluated (e.g., frailty, sarcopenia, nutritional status, other organ failure, infections) often contribute to AF. Finally, the role of graft steatosis and the protective effect of perfusion machines are yet to be analyzed in a large multicentric prospective study. These factors may hamper or contraindicate a timely and efficacious re-transplantation.

Methods: We call for an International, Prospective, Non-competitive, Observational study to validate-optimize prediction models of AF at 90 days and one year after LT by collecting data on current practice, various donor types (DBD, DCD, living donors [LD]) with balanced international enrollment, homogeneous center volume, and evaluation of various mitigation strategies (e.g., perfusion machines). An International Steering Committee has defined the study protocol. It includes both a prospective cohort (high-volume centers with >65 LT per year, 50 pts each) to develop new predictive models and a retrospective cohort (intermediate and low-volume centers, 75 pts each) to validate them. The retrospective enrollment will also be allowed to high-volume centers participating in the prospective cohort. Secondary objectives include: - developing a novel time-based dynamic algorithm, with increasing accuracy from day 3 to 7; - identifying an optimal time for re-transplantation; - investigating differences in AF among DBD, DCD, LD grafts; - evaluating strategies (e.g., perfusion machines) that mitigate AF; - evaluating the ability to predict complications (AKI, ischemic cholangiopathy) and mortality (futility threshold). The IMPROVEMENT study-protocol is registered on ClinicalTrials.gov, and available online at https://gemelligenerator.it/projects/the-improvement-study-2/.

The GANTT diagram is reported in Figure 3. We welcome the participation of additional transplant professionals to participate in this global collaborative, which will provide great insights into the multitude of factors impacting allograft dysfunction, and may establish kinetic risk prediction tools (L-GrAFT and EASE) as the most appropriate end-points in translational studies evaluating ischemia-reperfusion injury in liver transplantation.

### Abstracts

#### 413.12

**Summarizing the Characteristics of the Recent Progress of Organ Donation and Transplantation in China by Using GODT Data**

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**Introduction:** Although COVID-19 pandemic has caused a significant impact worldwide, organ donation & transplantation (OD & OT) practice continues in most of the countries. Since China launched the pilot program of voluntary deceased OD in 2010, the national organ donation & procurement system has been developing towards standardization. In this study, features of the global & national trends in OD & OT during the COVID-19 pandemic were summarized.

**Method:** A retrospective study using data from the global observatory on donation and transplantation (GODT) was conducted. We analyzed the collected data to obtain the results and conclusions.

**Results:** The summed-up characteristics covered different aspects and could be outlined as the followings: 1) The number of global OT has been increasing until the outbreak of COVID-19 pandemic in 2020. There were 129,681 OT performed worldwide in 2020, a decrease of 17.6% comparing to that of 2019. The percentage of China’s annual OT to the global OT number rose from 7.9% among in 2015 (10,057 cases) to 13.8% in 2020 (17,949 cases). 2) In China, joint-efforts have been made to achieve self-sufficiency of OT on the national level. The total number of OD exceed 5,000 in 2020, accounting for 14.5% of the global deceased OD. The China OD & OT program works orderly with implementation of prevention control policy under the pandemic. 3) DBD remains as the major source for OT worldwide while the number of DCD has been increasing in the recent year. With the lasting promotion of clinical practice in brain death diagnosis, the percentage of DBD in China has increased over the past five years. 4) The percentage of global living donor (LD) transplants has decreased year-on-year. With the implementation of deceased OD program in different Asian countries, living donation does not comprise the majority of organ source for OT in Asia. 5) The percentages of liver, kidney and lung transplantation in China were on the rise compared to the global total and the liver transplantation accounted for the highest proportion. 6) China’s OT activity ranks second in the world, but the PMP of deceased OD & OT is low, indicating rooms for improvement. 7) Innovative transplant approaches were explored worldwide to meet the increasing transplant demands. Efforts have been made in China to promote innovation for transplantation, examples can be seen, such as the fact that China completed ischemia-free liver/kidney/heart transplantation, and successfully performed the world’s first double-lung transplant with COVID-19 patient in 2020.

**Conclusion:** Summary of current features in OD & OT in China and worldwide were analyzed in this study. The degree of OT program development varies across the world but all making efforts to meet the ever-changing demands for transplants. Chinese reform on OD & OT marks it one of the countries contributing to the increase of OD & OT activities worldwide but still has room for improvement in operational efficiency.
Long-term (>1 Year) Rejection/TMA Free Survival of Kidney Xenografts With Triple Xenoantigen Knockout and Multiple Human Transgenes in Nonhuman Primates

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1Center for Transplantation Sciences, Massachusetts General Hospital, Boston, MA, United States; 2eGenesis Inc., Cambridge, MA, United States.

Pigs with deletion of 3 carbohydrate xenoantigens (triple knock-out, TKO) are expected to be optimal donors for human xenotransplantation. We hypothesized that concomitantly inserted human transgenes (hTGs) are important to attenuate anti-xenograft immune responses. In the current study, kidney xenotransplants from four TKO pig lines with different hTGs as well as TKO without hTGs were evaluated.

Nineteen cynomolgus monkeys received kidneys from four different TKO pig lines (TKO-A to D) with various expression of human immune regulatory proteins (ImmURPs), complement regulatory proteins (CompRPs) and coagulation regulatory proteins (CoagRPs) or no hTGs. Recipients were treated with anti-thymocyte globulin (ATG) and rituximab induction followed by anti-CD154 antibody (every 1-2 weeks) and daily mycophenolate mofetil (MMF). Prednisone and either rapamycin or tacrolimus were also administered for the first two months.

Two recipients of TKO-A, which expressed higher ImmURP with lower CompRPs, survived for 2 and 61 days, while recipients of TKO-B with high CompRPs and lower ImmURPs survived for 15, 20, 71, 135, 265 and 316 days (Table 2). 15 NHPs received xenografts from TKO-C with CompRP, ImmURP, CoagRPs TM/EPCR, and with or without endogenous retrovirus inactivation (RI). Ongoing recipients (7) show no signs of rejection or thrombotic microangiopathy (TMA), currently at days >489, >482, >292, >160, >104, and >48, treated with only anti-CD154 mAb and MMF after 2 months. Rejection and TMA appeared to contribute to graft loss in the remaining 8 recipients between 8 and 240 days following transplant. Both recipients of TKO-D, in which CoagRPs TM and TFPI were present, survived for 243 and 267 days without rejection or TMA but were euthanized due to infectious complications. Finally, both recipients of TKO without hTG lost their xenografts early on day 4 and 50, due to severe tubular injury and significant proteinuria (final pathologic diagnosis pending but AMR is suspected) respectively.

Prolonged (>1 year) rejection and TMA-free survival of kidney xenografts with TKO and multiple hTGs have been achieved. Whether the hTGs are essential for long-term xenograft survival remains to be determined with more control animals without hTGs. Our preliminary results that two recipients of TKO without hTG lost their xenografts early, suggest an essential role of hTGs for long-term xenograft survival.

Funding provided by NIH Grant 5T32AI007529-22 & eGenesis Inc.
Histological and Molecular Characterization of Kidney Xenografts Transplanted to Decedent Humans


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Background: Genetic modifications have recently permitted Xenotransplantation in decedent humans showing initial kidney function recovery. There is an unmet need and unprecedented opportunity for providing a precision phenotyping of these allografts to further optimize Xenotransplantation.

Methods: We report here the complete histological and immunological assessment of the first 2 Xenotransplants performed at NYU. Porcine renal Xenografts were procured from genetically engineered (α-Gal knockout) pigs. Kidneys were removed and wedged biopsied at 56 hours after transplantation and compared with non-transplanted genetically modified and WT pig kidneys. We performed a multiplex histological, histochemical consisting in staining for different cell types including CD20, CD3, CD15, CD68, NKP46 and C4d. Expression analysis of RNA samples was performed using the nCounter platform. To capture both the host immune response coming from the receiver with the tissue-related pig genes, we adapted the B-HOT panel from cross-species analysis between Xenograft and Human by assigning the orthologous genes between corresponding human and pig data sets. The differential expression analysis was computed using Wald test and significant genes were identified after adjusting for multiple comparisons (Benjamini-Hochberg method).

Results: Both Xenografts presented with glomerulitis lesions characterized by microvascular inflammation in glomerular capillaries composed by CD15+ and CD68+ macrophages cells. There were leukocytes infiltration of in peritubular capillaries of Xenograft #1 which involved < 10% of the cortex, while Xenograft#2 did not show ptc lesions. CD3+ T lymphocytes were very rare in glomeruli and interstitium and tubulitis was absent in both Xenografts. No C4d complement deposits was detected. Neither arteritis nor interstitial hemorrhage and thrombotic microangiopathy were observed (Figure 1). Both Xenografts showed acute tubular necrosis reflecting ischemia-reperfusion injury. Non transplanted kidneys from both Genetically modified pigs as well as wild type pigs did not show any abnormalities (Figure 1). Gene expression studies revealed in both Xenografts increased expression of biologically relevant genes related to injury repair response (APOE, TIMP1, IER5), endothelial activation (FGD2), effector T-cell (GIMAP5), IFN response (CALHM6, GBP5, IFTM1, IFTM3, JAK2, PSME1, SLAMF7, CXCL10), monocyte/macrophage activation (CD68, IFNGR1, IFNGR2, FCER1G), and humoral response (HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DRB3, CCL3/ L1), Figure 2.

Conclusions: This first multiplex xenograft assessment reveals adequate Xeno allografts without hyperacute rejection. However, we found a pattern of ongoing antibody-mediated rejection confirmed by gene expression showing increased expressing of injury genes as well as endothelial, macrophages and AMR genes. These results open avenues for future refinement and targets for improving xenograft both from allograft preservation to the control of the humoral harm of rejection.
Review of the Safety and Efficacy of Imunosuppression in the Pig-To-Nonhuman Primate Islet Xenotransplantation Model

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Background: With the recent progress of xenotransplantation moving to the clinic there is renewed enthusiasm in the field of xenotransplantation, but the need for strong immunosuppressive and anti-inflammatory agents remains. The effects and safety of these agents need to be reviewed in detail to allow progress to the clinic. This project aimed to evaluate the short-term (100 days) effects of immunosuppression on haematological and immunological parameters following neonatal porcine islet cell cluster (NICC) xenotransplantation in a diabetic non-human primate model.

Methods: Four baboons received 5 doses of anti-CD2 at 5mg/kg from day -3 to day 21 along with fortnightly anti-CD154 administration at 20-30mg/kg and belatacept administration at 20mg/kg. This was followed by daily maintenance immunosuppression of tacrolimus at 5mg/kg or sirolimus at 2mg/kg. Prior to immunosuppression administration, blood was collected to establish baseline haematological and immunological parameters. Full haematological parameters were assayed and immunological parameters including B cells, T cells, monocytes, and granulocytes were assessed by flow cytometry.

Results: The immunosuppressive therapy was highly effective in suppressing total white cell counts in all recipients. By day 100, B and T cells were depleted by 50-60% compared to baseline. In the 14-day gap between treatment with anti-CD154+belatacept, the immune cells (particularly B and T cells) recovered but were suppressed at each subsequent time point as compared to previous levels. There was a gradual reversal of the CD4:CD8 ratio, with a reduction of CD4+ cells and an increase in CD8+ cells over the 100 days. Tregs, a key component of achieving tolerance, gradually depleted by 50-60% compared to baseline. In the 14-day gap between treatment with anti-CD154+belatacept, the immune cells (particularly B and T cells) recovered but were suppressed at each subsequent time point as compared to previous levels.

Conclusion: This novel combination of immunosuppressive agents is effective and safe in baboons receiving neonatal porcine islet cell cluster xenotransplantation.
**414.5**

**Patient Selection for Pig Cardiac Xenotransplantation**

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**Background:** The first clinical genetically-engineered pig heart transplant has stimulated consideration of which patients might be medically and ethically appropriate to enroll in the initial clinical trials. Beyond exceptional ‘compassionate use’ applications, as in the University of Maryland case, which patients might be selected for formal ‘qualifying’ trials of ‘destination’ or ‘bridging’ heart xenotransplantation?

**Approach and Results:** Patients eligible for a heart allograft and in whom mechanical circulatory support is contraindicated or associated with a high risk of mortality or morbid complications, such as presence of a mechanical valve prosthesis, restrictive or hypertrophic cardiomyopathy, and refractory ventricular arrhythmias, are at high risk of dying before transplant, and might be eligible for either a ‘bridging’ or ‘destination’ trial. Patients with high titers of panel-reactive anti-HLA antibodies, including prior allotransplant recipients with graft vasculopathy, are at high risk of sudden death, experience long waiting times and inferior post-allograft survival, those without antibodies that cross-react with pig cells might expect better survival after a successful heart xenograft than after desensitization to enable a heart allograft. Infants and children with complex CHD have limited access to allotransplantation due to the scarcity of size-matched donor organs. In these patients the results of mechanical support are poor, and both survival and quality of life after multiple staged surgical reconstructive procedures remain limited, particularly for those relying upon univentricular ‘Fontan’ physiology. A genetically-engineered pig heart could be used as a life-supporting ‘bridge’ for a clinically deteriorating infant or child until a heart from a size-appropriate deceased human donor can be obtained. Pediatric or adult patients presenting in extremis and unable to participate, with their caregivers, in a complete, robust informed consent process would be inappropriate to enroll on ethical grounds. Patients whose prognosis is poor based on risk factors not directly related to their heart pathology, such as frailty or malignancy, that would disqualify them as heart allograft candidates should also be avoided, as this approach is likely to yield poor outcomes and undermine public and peer support for xenotransplantation.

**Conclusion:** We propose that patients meeting these inclusion and exclusion criteria are appropriate to consider for enrollment in initial heart xenograft clinical trials.

**RC** is supported by the Benjamin Research Scholarship from the German Research Foundation (DFG). DKCC and RNP receive grant support from the NIH (NIH NIAID U19 grant AI090059, and U01 grant AI153612), and the Department of Defense (grant W81XWH2010559; DKCC), and previously received research funding from Revivicor, a subsidiary of United Therapeutics. RNP has received research support from eGenesis and Tonix. LB and DE are part of Revivicor scientific team.

**414.6**

**Porcine ULBP1 Disruption Does Not Significantly Reduce Human NK Cell Activation and Cytotoxicity in an In Vitro Model**

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**Background:** Pig-to-human xenotransplantation has the potential to address the critical organ shortage. Genetically-engineered pig organs have significantly prolonged survival in human and nonhuman primates by overcoming hyperacute rejection. Human natural killer (NK) cell-mediated acute xenograft rejection of porcine endothelial cells has been established. Porcine UL-Binding Protein (ULBP1) has been identified as a porcine ligand of human NK cell activating receptor NKG2D; interactions presumably lead to NK cell activation and ultimately porcine cell cytotoxicity. We sought to improve pig-to-human compatibility by eliminating ULBP1 ligand in an immortalized porcine liver-derived endothelial cell line (ipLDEC) with five-gene knockout (5GKO). The 5GKO cell line has mutations in GTAA1/CMAH/VPgent2/SLA-I α-chain/I2M: three genes encoding enzymes responsible for xenotransplant production and two genes encoding swine leukocyte antigen class I.

**Methods:** CRISPR/Cas9 technology was used to knockout the porcine ULBP1 gene in the 5GKO cell line to create a ULBP1-KO/5GKO cell line. Human peripheral blood mononuclear cells (PBMCs) from four donors were activated with human IL-2 for 5 days. Human PBMCs were co-cultured with 5GKO, ULBP1-KO/5GKO, and Wild-Type (WT) ipLDECs. Cells were stained with antibodies to CD45, CD3, CD56, and CD107a. Flow cytometry analysis was gated on the CD3-CD56+ NK cell population and monitored for expression of human NK cell activating receptor NKG2D; interactions presumably lead to NK cell activation and ultimately porcine cell cytotoxicity. We sought to improve pig-to-human compatibility by eliminating ULBP1 ligand in an immortalized porcine liver-derived endothelial cell line (ipLDEC) with five-gene knockout (5GKO). The 5GKO cell line has mutations in GTAA1/CMAH/VPgent2/SLA-I α-chain/I2M: three genes encoding enzymes responsible for xenotransplant production and two genes encoding swine leukocyte antigen class I.

**Results:** Porcine ULBP1 gene mutation was confirmed by Sanger sequencing (Figure 1a), establishing a porcine ULBP1-KO/5GKO cell line. There is no statistically significant difference in NK cell activation between co-cultures of human PBMCs (n=4) with pULBP1-KO/5GKO and 5GKO ipLDEC using CD107a. (Figure 1b). There is no statistically significant difference in NK-induced cytotoxicity between co-cultures of human PBMCs (n=6) with porcine ULBP1-KO/5GKO and 5GKO cell lines using Calcein AM assays (Figure 1c). As expected, HLA-G+/5GKO cytotoxicity was decreased (p = 0.0189) compared to WT (Figure 1c).

**Conclusion:** We established a porcine ULBP1-KO/5GKO cell line. Our studies demonstrate no statistically significant difference in NK cell activation and NK cell-mediated cytotoxicity between 5GKO and ULBP1-KO/5GKO cell lines. Our studies show that ULBP1 is not a crucial ligand for human NKG2D. Future studies will target different human NK cell activating porcine ligands.
The Perioperative Cardiac Xenograft Dysfunction (PCXD) Has A Major Impact in (Life-Supporting) Orthotopic (oXTx) Cardiac Xenotransplantation, but Not in the Heterotopic Thoracic (htXTx) Xenotransplantation

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Introduction: With 50% perioperative cardiac xenograft dysfunction (PCXD) frequently occurred after ischemic crystalloid cardioplegia (Bretschneider) in oXHTx. This is a major hurdle for long-term survival in a life-supporting orthotopic cardiac pig-to-baboon xenotransplantation (XT) model (oXHTx). A great breakthrough was to prevented this by using a new non-ischemic cold preservation technique from Stig Steen. The oXHTx data of PCXD were compared with our previous heterotopic thoracic (htXTx) model. The common problem of the xenograft “over”growth (XOG) had to be solved with antiproliferative drugs.

Methods: In a group G1 (n=19) „piggyback heart” technique of htXTx from Barnard and Losman was used in baboons (2 with CD40Ab). OXTx using GalKO/hCD46/hTMtg pig hearts was performed in another 19 cases. Immunosuppression (IS) consisted of rituximab, ATG, mycophenolate, corticosterone and a CD40mAb for costimulation blockade. As an early cardiac low output the PCXD in the oXTx group G2 (n=5) was prevented in a group G3 (n=5) by using a new, non-ischemic cold perfusion (CP) technique with oxygenated blood. For xenograft overgrowth inhibition (XOGI) in a final preclinical group G4 (n=9) the mTOR inhibitor temsirolimus and antihypertensive drugs were applied.

Results: All baboons were weaned from ECC. Technical failures (n=5) in htXTx were excluded. In the htXTx model survival was 13 and 35 days with CD40Ab and without 2, 4, 7, 9, 12, 14, 16, 17, 19, 19, 37 up to 50 days. Survival after oXTx was 1 (n=4), 2 (n=2), 18, 27, 30, 40 days and G4 15, 27, 51, 90 (n=4), 182 and 195 days. Four baboons in htXTx group G1 died of delayed xenograft rejection (DXR) and sepsis due to an „over”-growth, 3 baboons in G2 died of PCXD with Brettschneider cardioplegia. After CP in G3 no PCXD was found and they died mostly of liver failure and cardiac overgrowth. In the preclinical group G4 combining CP and XOGI four baboons were terminated at day 90 and two survived 182 and 195 days, 2 died (d15, d27) of sepsis with pCMV-positive donor hearts. All baboons were in excellent general conditions. No hyperacute and DXR was found. PCXD was also registered in G1 (htXTx) in a low pressure curve inside the xenograft [n=3], but was in hemodynamics not relevant, because the baboons own heart supported during PCXD, which disappeared after 48 hours. In total the htXTx model was limited by a rapid growing pig heart in the small right thorax of the recipient compressing the right lung.

Conclusion: In the htXTx group G1 we could also find signs of PCXD indirectly, but it was not relevant and reversible after 2 days, but in oXTx it was a major problem. The essential progress is the CP and XOGI in terms of long-term survival, which now fulfills the ISHLT guidelines (90-days-survival of 60%) for a clinical phase I trial. CP was also used in the compassionate use patient in Baltimore 1/2022. Also other blood cardioplegic solutions like Buckberg, Calafiore or Del Nido must be tested for future XT.

SFB127 Xenotransplantation.
The Role of Co-expressing MHC Class I Molecules in Pig Endothelial Cells: A Case for HLA-E and HLA-G in Xenotransplantation

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Introduction: Pig-to-human xenotransplantation (XTx) is a promising solution to the organ shortage. Genetically-modified (GM) pigs lacking major xenoantigens have reduced hyperacute rejection and prolonged xenograft survival which further suggested XTx as a promising solution to the organ shortage. Despite these advancements, acute rejection remains a major barrier to clinical XTx. Natural killer cells (NK) play a crucial role in transplantation. In the context of XTx, suppressing human NK activity by expressing HLA class I molecules in pig organs may protect xenografts from host immune attack. Therefore, we aimed to (i) individually express HLA-C1, -E, and -G in a GM pig endothelial cell line null for five key xenoantigens (5GKO), (ii) co-express HLA-E and HLA-G in 5GKO, and (iii) evaluate human NK response to HLA class I+ 5GKO cells.

Methods: DNA sequences encoding HLA-C, -E, and -G were designed, synthesized, and cloned into expression vectors. Four GM porcine cell lines (5GKO.HLA-C1, 5GKO.HLA-E, 5GKO.HLA-G, 5GKO.HLA-E.HLA-G) were generated by transfection. IL-2-activated human peripheral blood mononuclear cells (PBMC) from five donors were co-cultured with GM porcine cell lines to initiate NK cell-mediated immune responses. Using flow cytometry, NK cell activation was evaluated by quantifying cell-surface expression of CD107a in the CD3-CD56+ cell population. Statistical analyses performed include one-way ANOVA and a post-hoc Tukey test.

Results: We successfully expressed HLA-C1, HLA-E, and HLA-G in 5GKO cells (Fig.1 A-C) and co-expressed HLA-E and HLA-G in 5GKO cells (Fig.1 D). Individual expression of HLA-C, -E, and -G did not demonstrate a significant difference in NK cell activation compared to control 5GKO cells; however, co-expression of HLA-E and HLA-G significantly reduced human NK cell activation compared to all other groups (Fig. 2).

Conclusion: Co-expression of HLA-E and HLA-G in porcine cells synergistically reduces NK cell-mediated cytotoxicity and shows promise for incorporation into GM pigs for pig-to-human xenotransplantation.

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Figure 1. A-C: Expression of cell-surface HLA-C1, -E, and -G in respective GM porcine cell lines; D: expression of cell-surface HLA-E and -G in novel 5GKO.HLA-E.HLA-G GM porcine cell line; 5GKO = GGTA1/CMAH/B4galNT2/SLA-I alpha chain/Beta2-microglobulin. GGTA1 = alpha-1,3-galactosyltransferase; CMAH = Cytidine monophospho-N-acetylneuraminic acid hydroxylase; β4galNT2 = Beta-1,4 N-acetylgalactosaminyltransferase 2; SLA-I = swine leukocyte antigen I α chain.
Shared Transcriptional Trajectory of Tissue Tregs Between Tolerant-Grafts and Lymphoid Organs in Transplant Tolerance

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Background: We found previously that depletion of CD4+Foxp3+Tregs at early time (within 20 days) and later time (80 days) of transplantation abrogated pig-islet-xenograft tolerance in mice induced by short-term CTLA4-Fc/MR-1 treatment. We also identified memory-like CD127+/highCD4+GFP+/Foxp3+Tregs (CD127+/highTreg) in spleen of tolerant mice following CTLA4-Fc/MR-1 induction and demonstrated their potent suppressive capacity in an adaptive-transfer model.

Aims: 1) Further characterise tissue CD127+/high Tregs. 2) Investigate transcriptional profile of CD4+Foxp3+Treg and non-Foxp3 CD4+ subsets in transplant tolerance.

Methods: We used DEpletion of REGulatory T cells (DEREG) mice, which carry the enhanced GFP transgene under Foxp3 promoter as recipients of NICC transplantation tolerance model. Cell-subsets were selected with FACS/Cell Sorter based on positive or negative expressions of CD4, GFP, and CD127 or CD45, CD4 and GFP. mRNA expression of Il-10, Tgf-β, Blimp-1, Ebi3 (reflecting IL-35) of CD127+/high Tregs was assessed using TaqMan® Gene Expression Assay. Bulk RNA-Seq revealed the transcriptional profiles of CD127+/highTreg, CD127-/low Treg, CD4+Foxp3 Treg, non-Foxp3 CD4+, and CD45+CD4- subsets from spleens (sp), graft draining-lymphocytes (DLN/dln), or grafts in mice with 100-day tolerant-graft induced by CTLA4-Fc/MR-1 blockade or naïve DEREG-mice.

Results: RT-PCR showed Ebi3, Il-10, Blimp-1 significantly increased in splenic CD127+/high Tregs compared to naïve-CD4+Foxp3+Tregs or non-Foxp3 CD4+ T cells. The proportion of CD127+/high Tregs was higher in tolerant grafts (25.6±3.1%) than tolerant spleens (14.8±0.4%). 15 pairwise-comparisons identified 1740 differentially expressed genes (DEGs) (FDR<0.05) that clearly distinguished between CD45+CD4-, Foxp3-CD4+T, and Treg subsets; with no striking differences seen for CD45+CD4- cells (spleen) and mild differences in Foxp3-CD4+T cells (spleen) between naive and tolerant-groups; and diverse differences within Treg subsets. Next, 9 paired cross-comparisons between different Treg subsets identified 427 DEGs and showed large difference between graft-Treg and Treg subsets of spleen or DLN; moderate differences between spTreg and dlnTreg subsets; and minor differences within the three Treg subsets of spleen or DLN. Further, compared to naïve-Treg or CD127-low Treg subsets, graft-Tregs shared many upregulated-DEGs across dlnCD127+/high Treg, and/or spCD127+/high Treg including Ilt7, Kctd12, Cxcr6, Cilia2a, Anxa1, H2-Ab1 (an MHC-II gene), Klrk1, Klrk1, Ccl5, Id2, Ccr2, Adam8, Il18r1, Il1r1 that have been reported in multiple tissue/tumour Treg subsets with memory features and high suppressive functions in both mice and/or humans.

Conclusion: Tissue-Tregs (CD127+/high Tregs) developed in graft, spleen and DLN of transplant-tolerant mice share a transcriptional trajectory with other tissue/tumour Tregs.
Cytokine Analysis of First Gal-KO Renal Xenotransplantation From a Pig-To-Human Recipient

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Background: Xenografts from genetically modified pigs have become one of the most promising solutions to the human organ shortage. Humans lack the \(\alpha_1,3\)-Gal glycan ubiquitously expressed on pig cells. Naturally occurring anti-\(\alpha_1,3\)-Gal antibodies can cause hyperacute rejection of porcine xenografts. Cytokine levels change in response to systemic inflammatory or transplant environments. We report the first instance of cytokine analysis from xenotransplantation of a kidney from an \(\alpha_1,3\)-Gal knock-out (KO) pig to a recently deceased human.

Methods: Under a protocol approved by the NYU institutional committee two xenotransplants were performed in late 2021 on brain-dead recipients who consented their bodies for organ and research donation, but were found to have organs unsuitable for transplantation. Kidneys from \(\alpha_1,3\)-Gal KO pigs were transplanted into the thigh of the recipient. Immunosuppression consisted of methylprednisolone and mycophenolate mofetil until the kidneys were explanted at 54 hours. Cytokine analysis was performed as well as genetic expression for cytokines in the blood and for the second transplant biopsy tissue as well. Blood cytokines were measured in the NYU clinical laboratory. Xenotransplant tissue was obtained by needle biopsy and mRNA extracted for analysis.

Results: The xenografts immediately appeared pink and well-perfused and began to make urine. The cold ischemic times were 7 and 6 hours, respectively. Most cytokines showed no change or were undetectable in the blood. Of the detectable cytokines, IL-2 mRNA levels decreased in porcine kidney biopsy samples over the course of the second transplant but increased in the blood (this recipient had a positive CDC xenocrossmatch).

Conclusions: Our study served as proof of concept that \(\alpha_1,3\)-Gal KO organs can be transplanted into humans without the risk of accelerated rejection and cytokine storm. Further analysis and correlation between xenotransplant porcine tissue biopsy and circulating blood levels is warranted in future preclinical studies.

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414.11
Cross-Reacting Antibodies in Xenotransplantation

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Introduction: Before initiating clinical trials of pig kidney or heart xenotransplantation, important questions need to be addressed. (i) Will a patient with a high level of anti-HLA antibodies be at increased risk of rejecting a pig organ graft? (ii) Will a pig organ graft successfully bridge a patient to allotransplantation without an increased risk of rejecting the allograft.

Methods: The literature was reviewed regarding relevant reports of in vitro and in vivo studies in nonhuman primates (NHPs) and humans, but not in other species. In most studies, serum anti-pig antibodies were detected using pig RBCs or PBMCs, and their effect confirmed by a complement-dependent cytotoxicity assay. Allotransplantation after pig xenotransplantation/sensitization studies were limited to (i) pig-to-NHP models, (ii) human subjects exposed to pig antigens during ex vivo pig organ perfusion before allotransplantation, and (iii) immunosuppressed patients with renal allografts who received fetal pig islet-like cells.

Results: Studies in HLA-sensitized subjects: Nine studies reported that cross-reactivity between the anti-HLA immune response and pig antigens are, or may be, detrimental to survival of a xenograft, and four studies reported no detrimental effect. The data suggest that approximately 11% of highly HLA-sensitized wait-listed patients demonstrate cross-reactive antibodies, representing only 2% of all wait-listed patients.

Studies of allotransplantation after sensitization to pig antigens: NHPs exposed to pig antigens (n=72) did not become sensitized to alloantigens and did not show an increased incidence of allograft rejection. Humans (n=14) exposed to pig antigens by ex vivo perfusion of pig organs before allotransplantation showed no definitive features of early allograft rejection. Patients (n=10) with Type 1 diabetes with functioning renal allografts who received wild-type fetal pig islet-like cells developed xenoreactive antibodies against Gal antigens without any increase in panel-reactive antibodies or detrimental effect on allograft function.

Conclusion: (i) All patients for whom xenotransplantation is being considered should be tested to ensure that they do not have antibodies against pig RBCs and/or PBMCs. This is particularly important in those with high anti-HLA antibody levels (a high cPRA). (ii) Although based on limited evidence to date, there is little or no risk that previous sensitization to pig xenoantigens is detrimental to subsequent allotransplantation.

414.12
Potent Suppressive Function of Xeno-Antigen Reactive Human HLADR+CD27+Tregs via Enhanced CD95 and ICOS Expressions

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Background: We previously identified xenogeneic antigen-reactive human HLADR+CD27+Tregs with enhanced suppressive function in vitro and more capable of suppressing islet xenograft rejection in a humanised mouse model of neonatal porcine islet cell clusters (NICC) transplantation.

Aims: (1) Phenotyping HLADR+CD27+Tregs and 2) evaluating possible pathways through which they exert a suppressive activity.

Methods: Human CD4+CD25+hiCD127-Tregs isolated from peripheral-blood-mononuclear-cells (PBMCs) were co-cultured with irradiated porcine PBMCs for three subsequent cycles in the presence of IL-2/rapamycin and anti-CD3/CD28 beads. At day 21, phenotyping HLADR+CD27+Tregs of expanded Tregs was performed using flow cytometry for both surface- and intracellular expression (MFI) of the transmembrane proteins CD95, ICOS, CTLA-4, GITR; surface expression of CD39 and CD62L; and intracellular expression of FOXP3 and Helios compared to CD27-, HLADR-, HLADR-CD27-, HLADR+CD27-, HLADR+CD27+, depleted-HLADR+CD27+Treg subsets or all expanded Tregs.

Results: There are no differences of FOXP3 and CD39 expression on HLADR+CD27+Tregs compared to all other subsets. CD62L increases significantly on HLADR+CD27+Tregs when compared to HLADR+CD27+ and more HLADR+CD27+Tregs with enhanced suppressive function HLADR+CD27+Tregs compared to all other subsets. CD62L increases significantly on HLADR+CD27+Tregs when compared to HLADR+CD27- and HLADR-Tregs. We previously identified xeno-antigen reactive human HLADR+CD27+Tregs with enhanced suppressive function in vitro and more capable of suppressing islet xenograft rejection in a humanised mouse model of neonatal porcine islet cell clusters (NICC) transplantation.

Conclusion: The enhanced suppressive function of xeno-antigen reactive HLADR+CD27+Tregs is associated with enhanced expression of CD95 apoptotic antigen and ICOS costimulatory molecule. HLADR and CD27 are the important immune checkpoints for xeno-antigen specific Tregs.
PGC1alpha-Mediated Metabolic Reprogramming Facilitates M1 Macrophage Polarization During Steatotic Allograft Dysfunction After Liver Transplantation

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Introduction: The pro-inflammatory macrophage activation is the major force to allograft dysfunction, but detailed mechanism is poorly understood. Our previous study demonstrated the pivotal role of PGC1α in mediating steatotic graft injury via mitochondrial regulation (Liu et al., 2020). This study aims to elucidate the role of PGC1α in regulating macrophage polarization regarding metabolic reprogramming during steatotic graft injury.

Method: Intrahepatic PGC1α expression and macrophage subpopulation were quantified and their correlation with acute phase steatotic allograft dysfunction and long-term graft survival was analyzed in a liver transplant cohort. Macrophage subtypes with distinct PGC1α expression patterns were investigated in a rat orthotopic liver transplant model. The functional study of PGC1α in mediating macrophage metabolic reprogramming as well as its polarization were studied in a mouse ischemia and reperfusion model.

Results: The cutoff value of intrahepatic PPARGC1A (PGC1α) mRNA level (relative fold change=0.385) was determined by the ROC curve with AUC of 0.811 (p<0.001) (Fig. 1A). Divided by PGC1α cutoff, lower expression recipients using steatotic grafts were shown significantly deteriorated long-term graft survival as well as acute phase elevation of ALT and AST (Fig. 1B-1C). The cytokine quantification showed that patients with early allograft dysfunction (EAD) had both cellular and humoral pro-inflammatory response, which were indicated by increased CD68 and TNFα expression in the graft and elevated IFNγ but decreased IL10 concentration in the plasma (Fig. 1D-1E). Further consolidated by the rat liver transplant models, steatotic graft had a higher M1 macrophage ratio but lower M2 ratio (Fig. 2A). Especially, the subgroups of CD68+IFNγ+PGC1αlow macrophage and CD163+PGC1αhigh macrophage were both higher in the steatotic graft compared with the normal graft (Fig. 2B). Detailed metabolism analyses showed that steatotic graft had down-regulated oxidative phosphorylation (OXPHOS) but enhanced glycolysis, which were indicated by increased plasma lactate level and decreased OXPHOS complex II (succinate dehydrogenase, SDH) activity (Fig. 2C-2D). Functional study showed that inhibition of PGC1α decreased the expression of OXPHOS subunits Sdha and Coxii, but reactivation of PGC1α restored their expression (Fig. 2E). Consistently, inhibition of PGC1α in liver showed elevated ALT and AST, exacerbated portal triad inflammation, as well as extended steatosis and apoptosis, whereas reactivation of PGC1α attenuated these phenocena (Fig. 2F-2G).

Conclusion: PGC1α is pivotal in mediating steatotic graft injury via promoting intrahepatic M1 macrophage polarization through metabolic reprogramming.

Reference
TUM012 – A New Polymer for Ex Vivo Allograft Coating To Minimize Post-reperfusion Thromboinflammation in Kidney Transplantation

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Introduction: Ischemic reperfusion injury (IRI) can trigger a detrimental thromboinflammation that impacts post-transplant outcome. This response is often a result of direct interaction between effector molecules of the innate immune system and altered endothelial and epithelial cell surfaces of the allograft. TUM012, a polymeric construct of polyethylene glycol (PEG) conjugated to a lipid anchor, was developed for ex vivo graft administration to enable a stable and transient cell surface coating to reduce an IRI-induced thromboinflammation.

Method: Compiled selected data on two pre-clinical transplant studies are presented: 1) Six pigs underwent allogeneic en-bloc kidney transplantation. The en-bloc kidneys were retrieved from 6 donor-pigs after exposure to 3-5 min in situ warm ischemia followed by 24 hours cold ischemia. Pre-transplant, both kidneys within the en-bloc package were randomly assigned to FITC-conjugated TUM012 (at 2 mg/ml) and vehicle. Post-reperfusion consecutive blood (from graft vein) and tissue samples from both kidneys were taken during an observation period of 6 hours. 2) Ten kidney allografts from 5 donor pigs were exposed to in situ warm ischemia and cold ischemia (as study 1) and randomly assigned to 2 groups receiving either TUM012 (n = 6) or vehicle (n = 4). In both studies, TUM012 was given exclusively locally to preserved kidney allografts. Post-reperfusion, local consecutive blood (from transplant vein) and tissue samples were taken intraoperatively. Native bilateral nephrectomy was performed in all recipient animals. Systemic Blood sampling continued daily for a total observation period of 4 days. Biomarkers of thromboinflammation (C5b-9, C3a and thrombin-complex), cytokines release as well as serum creatinine were measured.

Results: Effective, non-toxic and transient coating on both endothelial and epithelial cells can be achieved by ex vivo administration of TUM012 to retrieved kidney allograft (fig 1a, b). This ex vivo coating was associated with a marked reduction of an instant post-reperfusion thromboinflammation (IPRT) that occurred within the graft (fig 1c). Furthermore, TUM012 effectively reduced systemic release of cytokines (fig 1d) as well as improved kidney function post-transplant.

Conclusion: Here, we present selected data from an extensive pre-clinical assessment showing that ex vivo coating of kidney allografts with TUM012 seems to be safe and effective to reduce both the IPRT and the systemic cytokine release post-transplant. Consequently, this was associated with improved short-term kidney function. Currently, in a first-in-human study (ATMIRe), TUM012 is being evaluated for its safety and efficacy to reduce IPRT and to preserve kidney function in patients undergoing deceased-donor kidney transplantation at Skåne University Hospital in Malmö, Sweden.

AP39 Administration During Normothermic Ex Vivo Kidney Perfusion Reduces Preservation Injury

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Background: Normothermic Ex-vivo kidney machine perfusion (NEVKP) is a novel preservation technique for marginal kidney grafts. We recently determined that NEVKP preserves the expression of key proteins involved in mitochondrial biogenesis in kidneys, which could explain the improvement in graft function. We hypothesize that supplying oxygen during ex vivo machine perfusion will replenish energy levels in mitochondria, thereby restoring mitochondrial function and reducing injury in marginal kidney grafts. AP39, a mitochondria-targeted hydrogen sulfide donor, has been shown to stimulate mitochondrial electron transport and improve cellular bioenergetic function. Here, we investigated whether the supplementation of AP39 during NEVKP protects mitochondrial function and improves renal grafts against ischemia reperfusion injury.

Methods: Porcine kidneys were exposed to 60 min of warm ischemia followed by 5 hrs of static cold storage (SCS) or NEVKP. The swine were divided into three groups: the SCS group, the NEVKP group, and a third group in which AP39 was additionally administered during NEVKP (NEVKP + AP39). After contralateral nephrectomy, grafts were auto-transplanted and animals were followed for 3 days. Renal and mitochondrial function were assessed and compared between groups.

Results: All animals survived the follow-up period in all 3 groups. Grafts preserved with NEVKP had lower serum creatinine (Scr) on postoperative day 3 compared to the SCS group. Treatment with NEVKP + AP39 further reduced Scr when compared to the NEVKP group (Scr of SCS vs NEVKP vs NEVKP + AP39: 11.7±0.7 mg/dl vs 8.1±1.3 mg/dl vs 4.1±0.8 mg/dl, mean±SD). This was also true for BUN on postoperative day 3 (BUN SCS vs NEVKP vs NEVKP + AP39: 125±21.7 mg/dl vs 64.7±23.5 mg/dl vs 27.3±2.9 mg/dl). We have performed ATP assay analysis on biopsy-derived cell suspensions from SCS and NEVKP stored grafts. Both ATP levels were increased in the NEVKP group compared with SCS group at the time of pre-implantation (ATP SCS vs NEKV: 25.6±10.6N/M/100000cells vs 114.8±10.3N/M/100000cells).

Conclusion: For grafts after prolonged warm ischemic time, NEVKP has shown to have the potential to improve mitochondrial function. Future studies will determine whether administration of AP39 during machine perfusion facilitates organ preservation by further preserving mitochondrial function.
415.4

Ischemia Minimization Improves Cardiac Function in an Ex Vivo Xeno Working Heart Model

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Introduction: Previous studies showed that ischemia minimization (IM), accomplished by perfusing the heart xenograft during storage, prevents 'initial cardiac xenograft dysfunction' (ICXD) and enables prolonged survival following orthotopic cardiac xenotransplantation. Here we report initial observations in a model designed to evaluate effects on heart performance associated with IM and genetic modifications targeted to address xeno-injury mechanisms in a working ex vivo model of ICXD.

Method: Hearts from genetically modified and wildtype (WT) pigs were procured after flushing with cold preservation solution (UW, 4°C) and stored for 3 hours either in cold saline (0.9%, 4°C: cold storage (CS)) or were perfused with oxygenated STEEN Solution with RBCs (IM). IM perfusion at 40 mmHg was initiated at room temperature for 20 minutes to facilitate homogeneous graft perfusion before cooling to 4°C for the remainder of the storage period. The genetically modified hearts either had combined knockouts of three specific xenogeneic carbohydrate genes (GTKO, CMAHKO, b4GALNT2KO: TKO) with variable expression of human transgenes (hTG) including complement and thrombo-regulatory proteins (n=29); or GTKO with additional expression of hCD55 (GTKO.hCD55; n=3). Heart function and laboratory parameters were assessed at specific timepoints on a working heart rig while perfused with freshly collected heparinized whole human blood. Troponin I was used as a marker for myocardial injury.

Results: In total, 41 hearts were perfused ex vivo, 23 after CS (TKO + hTG n=14, GTKO.hCD55 n=2, WT n=7), and 18 after IM (TKO + hTG n=15, GTKO.hCD55 n=1, WT n=2). Cardiac output (mL/min) was significantly improved for the IM group at all loading conditions relative to CS, (see figure 1). There was a strong trend toward reduced troponin I release, particularly within the first 60 minutes of perfusion (see figure 2).

Conclusion: IM is protective with respect to cardiac function following pig heart ischemia and subsequent reperfusion with human blood in an ex vivo model of heart xenotransplantation. The hypothesis that variation in physiologic and biochemical outcomes within groups is influenced by variable expression of complement and coagulation pathway regulatory genes is being investigated.
415.5

A Proof of Principle Study of Cell Targeted Delivery of SiRNA Guided by Innate Repair Receptor EPOR/betacR Highly Expressed by Injured Tubular Epithelial Cells in Porcine Kidneys Subjected to Extended Cold Ischaemic Times

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Introduction: Small interfering RNA (siRNA) has been used in biological models for disease modification. Whilst challenges remain with targeted cell delivery, caspase-3, an executing enzyme of apoptosis and inflammation, plays a crucial role in acute kidney injury. Using caspase-3 siRNA or erythropoietin derived peptide CHBP, we have demonstrated renoprotection against ischaemia-reperfusion injury in isolated kidney preservation, and further applied the conjugate of both.

Methods: Porcine kidneys (n = 3) subjected to 10 minutes of warm ischemia were retrieved and perfused with 500mL hyperosmolar citrate. In comparison with the control (Kidney 1) caspase-3 siRNA-HBSP (Kidney 2) or CHBP (Kidney 3) conjugate was administered into the kidney and autologous blood, and stored for 22 hours in ice. Organs were then preserved by normothermic perfusion (NP) for 3 hours using clinical-grade cardiopulmonary bypass. Functional parameters were recorded, and kidney biopsies were taken at time zero (pre-perfusion) and hourly intervals following NP.

Results: Preliminary findings showed increased arterial flow rate and urine output together with neutralised perfusate pH in the kidneys (2 and 3) receiving both conjugates compared to the control.

Conclusion: Improved physiological outcomes in kidneys subjected to the novel agent treatment suggest protective effects against ischaemia. We hypothesise outcomes should be transferrable to human kidneys, which may facilitate the use of marginal kidneys following prolonged ischaemia, otherwise deemed unsuitable for transplantation. Renal histological and molecular studies of the effect of the agent are underway.

415.6

Exploring Cell-Specific Mechanisms of Ischemia/Reperfusion Injury Mediated Reactivation of Cytomegalovirus From Latency in the Orthotopic Mouse Lung Transplantation

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Purpose: Cytomegalovirus (CMV) is the most common opportunistic infection in lung transplant recipients, with the highest risk seen in CMV seronegative recipients (R-) of seropositive organs (D+). This study aims to explore key molecular pathways responsible for transplant-mediated CMV reactivation by using single-cell RNA sequencing (scRNA-seq) in a mouse model of syngeneic D+/R- lung transplantation.

Methods: Left lungs from naive (D-) mice or MCMV latently infected (D+) mice were transplanted to syngeneic R- recipients, while the contralateral right lungs served as controls. Lung tissues from the transplants at day 2 post-transplant (POD) or controls were harvested for viral RNA analysis and single cell isolation. CD31+ and CD45+ enriched single cell suspensions were processed using 10X Genomics, followed by sequencing. The sequenced data were processed using Cell Ranger pipeline and Seurat. Additional transplants were treated with small molecule Myd88 inhibitor to determine whether innate immunity plays a role in transplant induced CMV reactivation.

Results: MCMV IE-1 mRNA transcripts were significantly upregulated at POD 2, but were not detectable in the controls, indicating that transcriptional activation is induced in the early phase of transplant and ischemia/reperfusion injury associated with the transplant procedures is an important contributing factor. In addition, viral DNA amplification was detected in the salivary glands of D+/R- recipients at POD14, confirming that transplant of a D+ graft results in viral reactivation and dissemination. These data support the mouse lung transplant model as a viable approach to study mechanisms of CMV reactivation. Data from scRNAseq analysis showed distinct lung and immune cell clusters in lung transplants and controls. There were minimal differences in transcriptome landscapes between D- and D+ lungs prior to transplant (controls). In contrast, the differences were prominent between lungs from D+/R- transplant vs D+/R- lung grafts in the myeloid populations (e.g. neutrophils, macrophages (Macs)) and endothelial cells. Gene expression of Macs showed more differences between transplant lungs and control lungs than any endothelial cells or neutrophils. Pathway analysis of differentially expressed genes for myeloid cell types showed several significant immune response pathways including MIF regulation of innate immunity and communication between innate and adaptive immune cells. Expression of Myd88 and c-fos were increased in the lung grafts regardless of latent MCMV infection. Furthermore, our preliminary study using a Myd88 inhibitor showed a trend of CMV viral load reduction in lung grafts.

Conclusions: Early I/R injury following lung transplant resulted significant alterations of transcriptome landscape unique to different cell types. Myd88/AP-1 plays a critical role in CMV reactivation; thus targeting Myd88 has a great therapeutic potential to prevent I/R injury-mediated CMV reactivation. NIH NIAID R21AI163876. NIH/NIAID P01AI112522.
Impact of HLA-A,B DR and DQ on Deceased Kidney Transplant Outcomes in the Tacrolimus/MMF Era: An Artificial Intelligence Approach

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Introduction: One of the biological barriers that can impact outcomes in kidney transplantation is HLA mismatch. Several immunotherapy protocols were implemented to reduce this detrimental effect. The aim of our study is to assess the effect of HLA mismatches on acute rejection rates and graft survival in the Tacrolimus era. Moreover, to determine the most important factors affecting survival.

Methodology: All kidney transplant patients registered in UNOS database between 01/01 2005 and 01/12/2019 were retrospectively reviewed. Inclusion criteria: deceased donor transplants that were discharged on Tacrolimus/Mycophenolate Mofetil. Exclusion criteria: multiple organ transplants, previous kidney transplants, recipient age<18 years old, living donor transplants, missing data about induction therapy, missing HLA mismatch or ABO incompatible transplant. We used double-selection lasso (least absolute shrinkage and selection operator) logistic regression model to assess for the effect of HLA-A, B, DR, and DQ on acute rejection rates at one-year post-transplant. Variables of interest were HLA-A,B,DR and DQ mismatch. Variables Lasso selected from were: recipient characteristics (age, sex, BMI, ethnicity, diabetes, recipient/donor CMV status, pre-transplant dialysis), donor characteristics (KDPI score) and transplant characteristics (induction therapy, steroid intake, cold ischemia time, delayed graft function, PRA). Acute rejection was defined as biopsy proven or clinically suspected rejection. For survival analysis, we fit a penalised Cox model after choosing best alpha. Cross-validated grid-search was used to evaluate the best alpha. The variables included in the penalised cox model: donor, recipient and transplant factors. We visualised the coefficients variations across different α using ridge regression model in figure 1.

Results: 66,021 were included. Worse acute rejection rates at one-year post-transplant were noted with incremental increase in HLA-DQ (Two HLA-DQ: OR=1.24, P=0.005, 95%CI:1.10-1.40; One HLA-DQ:OR=1.19,P=0.01, 95%CI:1.06-1.33), HLA-DR mismatches (Two HLA-DR: OR=1.41, P<0.01, 95%CI:1.25-1.61; One HLA-DR: OR=1.27,p<0.01, 95%CI:1.13-1.43),Two HLA-B (OR=1.19,P=0.049) and HLA-A(Two HLA-A: OR=1.18, P=0.01; One HLA-A: OR=1.16,P=0.02). In the penalized cox regression model, only Two HLA-DR mismatch was associated with worse survival (HR=1.13, P<0.01, 95%CI: 1.05-1.21). KDPI was the most important factor affecting graft survival (KDPI>80%: HR=2.3, P<0.01; KDPI 60-80%: HR=1.57, P<0.01; KDPI 40-60%: HR=1.23, P=0.01). Delayed graft function affected graft survival by HR=1.50 (P<0.01). Mean follow-up time was 3.79 years.

Conclusion: HLA-DQ, DR,B and A mismatches play a vital role in the occurrence of acute rejection in the Tacrolimus/MMF era. However, only 2-HLA-DR mismatch has significant effect on graft survival. KDPI>60% and delayed graft function play the most important role in determining graft survival.
416.2

Early Clinical Complications Following HLA-Incompatible Living Donor Kidney Transplantation

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Introduction: Incompatible living donor kidney transplant (ILDKT) recipients require desensitization to facilitate transplantation across donor-specific antibody (DSA); however, this substantial upfront immunosuppression may result in higher risk of early complications following surgery.

Method: We compared 682 ILDKT to 5685 compatible LDKT (CLDKT) Medicare-primary recipients drawn from a 25-center cohort with novel link-age to the United States Renal Data System from 1999-2014. We characterized DSA strength as positive-Luminex, negative-flow crossmatch (PLNF, n=129); positive-flow, negative-cytotoxic crossmatch (PFNC, n=349); or positive-cytotoxic crossmatch (PCC, n=204). Diagnoses of deep vein thrombosis (DVT), wound infection, hemorrhage, sepsis, pneumonia, and urinary tract infection (UTI) were ascertained using ICD-9 codes. We used propensity score weighted Cox regression models to quantify the risk of early complications in the first three months, and from three months to one-year post-transplant.

Results: Compared to CLDKT recipients, ILDKT recipients had higher incidence of DVT (14.4% vs. 8.4%), wound infection (15.0% vs. 8.7%), hemorrhage (19.2% vs. 9.3%), sepsis (27.7% vs. 20.8%), pneumonia (35.5% vs. 22.9%), and UTI (44.7% vs. 33.5%) (p for all comparisons<0.001) (Figure). Within the first three months, a higher risk of DVT (wHR PLNF=0.05, 0.45-3.93; PFNC=1.79, 0.39-8.05; PCC=1.88, 1.01-3.48), wound infection (wHR PLNF=0.08, 1.25-1.25; PFNC=1.60, 0.35-7.60; PCC=1.89, 0.90-3.93), and hemorrhage (PLNF=1.11, 1.96-4.29; PFNC=1.82, 0.95-3.46; PCC=2.96, 1.31-6.70) were observed across varying levels of DSA strength; however, the risk of these complications decreased thereafter. Although there was no evidence of increased risk of sepsis with the first three months, this risk subsequently increased (PLNF=1.11, 1.96-3.47; PFNC=1.24, 1.57-1.99; PCC=0.80, 1.69-3.62). In contrast, there was higher risk of pneumonia that persisted throughout both time periods (0-3 months wHR PLNF=0.89, 0.62-1.26; PFNC=1.14, 0.92-1.42; PCC=1.34, 0.80-2.29) was observed across varying levels of DSA strength; however, this substantial upfront immunosuppression may result in higher risk of early complications following surgery.

Conclusion: Providers should consider these risks during pre-operative counseling, and awareness may aid to improve protocols for ILDKT patient management.

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416.3

Are HLA-A,B,DR and DQ-Mismatching Important for the Kidney Allocation Schemes? UK Registry Data- an Artificial Intelligence Approach

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Introduction: Currently, there is inconsistency among different kidney allocation systems for deceased donors and paired exchange schemes in terms of assessment for HLA-A,B,DR and DQ mismatch. The aim of our study is to assess the effect of HLA-A,B,DR and DQ mismatch on kidney transplant graft survival in the current era.

Methodology: All renal transplant patients registered in the United Kingdom Transplant Registry database between January 2005 till January 2015 were retrospectively reviewed. Patients with complete data about HLA-A,D,DR and DQ mismatch were included. Follow up was till April 2021. Patient with complete dataset were included in the study. Recipients with multiple organ transplant, previous renal transplants, or those with missing data about HLA mismatch were excluded from the study. For survival analysis, we fit a penalised Cox model to the entire set of data. We obtained the estimated set of alphas using estimated cross-validated grid-search. The variables included in the penalised cox model donor, recipient and transplant factors in addition to the HLA mismatches. Then we determined the set of alpha for evaluation using optimized cross-validated grid-search. Moreover, we visualised how the coefficients changed for varying alpha using ridge regression model. The regression models were adjusted for recipient factors (age, sex, ethnicity, diabetes, body mass index), transplant factors (HLA mismatches, calculated reaction frequency, cold ischemia time, delayed graft function, induction, and maintenance immunotherapy) and donor factors (donor type, donor creatinine at time of retrieval, donor age).

Results: Median follow-up was 7.5 years. Among living donor kidney transplant recipients (n=4782), Incremental increase in HLA-DR mismatch touched statistical significance and was associated with worse survival (Two HLA-DR: HR=1.31, P=0.05, 95%CI: 1.0-1.7; One HLA-DR mismatch: HR=1.21, P=0.05, 95%CI: 1.00-1.47). None of the other categories of HLA mismatches were associated with worse graft outcomes (P>0.05 for each category). Other factors that played an important role in determining graft survival were delayed graft function (P<0.01), black ethnicity (HR=1.88, 95%CI:1.45-2.51, p<0.01), and donor age (HR=1.02, P<0.01). Among deceased donor kidney transplant recipients (n=7996), None of the HLA mismatches were associated with worse graft survival (P>0.05 for each category of HLA mismatch). The factors that played an important role in determining graft survival were delayed graft function (HR=1.94, 95%CI: 1.67-2.03, P<0.01), black ethnicity (HR=1.42, 95%CI:1.21-1.65, p=0.01) donor age (HR=1.02, P=0.01), and recipient age (HR=0.99, P=0.01).

Conclusion: In the current era, HLA-DR mismatches are associated with worse graft outcomes among living donor transplants. However, none of the HLA mismatches are associated with worse graft outcomes among deceased donor kidney transplant recipients. Other factors that play an important role in determining graft survival are delayed graft function, donor age and black ethnicity.
ANTI-HNA-3 Antibodies in Kidney Transplant Rejection: Is It an Immunological Risk Factor?

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Introduction: Human neutrophil antigens 3 (HNA-3a and HNA-3b) are located on choline transporter protein 2 (CTL2) and expressed on neutrophils, lungs, kidneys and other human tissues. Alloantibodies directed against these antigens are formed from allogeneic exposure and are mainly associated with transfusion-related acute lung injury (TRALI) and immune neutropenias, however due to the presence of this antigen in renal tissue and the doubt that HNA-3 alloimmunization may also be involved in cases of kidney transplant rejection, the study of the frequency of anti-HNA-3 antibodies in this context becomes a focus of great clinical relevance.

Objective: Investigate the presence of anti-HNA-3 antibodies in the serum of patients who had kidney transplant rejection.

Materials and Methods: A total of 604 patients with kidney transplant rejection were included in the study. The Granulocyte Agglutination Test (GAT) was performed as a screening test in all individuals included in the present study with a panel of granulocytes from at least three individuals previously genotyped for all HNA systems. Positive samples in GAT were tested using the microsphere-based technique (LABSCreen Multi kit, One Lambda); we analyzed the normalized background values ≥ 10 and immunofluorescence ≥ 1000 as a positive result for HNA-3 antibodies. HNA-3 genotyping by PCR-RFLP was performed only in individuals who had a positive result in serological techniques.

Results: We detected 85/604 (14.1%) positive samples in GAT and 11/85 positive samples in both GAT and LSM multi for anti-HNA antibodies. Regarding the specificity of these 11 samples, 6 (54.5%) individuals presented an anti-HNA-3b antibody confirmed by genotyping (HNA-3a/ HNA-3a). In addition to the anti-HNA-3b antibodies, other specificities of anti-HNA antibodies were also identified: 1/11 (9.1%) anti-HNA-1a, 2/11 (18.2%) anti-HNA-1b, 1/11 (9.1%) anti-HNA-FCγRIIIb and 1/11 (9.1%) anti-HNA-2. Furthermore, 14/85 (16.5%) individuals had anti-HLA antibodies detected by LSM multi: 8/14 (57.1%) class I, 3/14 (21.4%) class II and 3/14 (21.4) class I and II. No patient presented simultaneously anti-HNA and HLA antibodies.

Conclusion: Our data show that HNA-3b alloimmunization has a greater tendency in patients who rejected kidney transplantation compared to healthy blood donors (1.0% vs. 0.2% respectively, p=0.05). These findings indicate that the detection of anti-HNA-3b antibodies may allow a better understanding of patients’ immune response against renal allograft when no HLA antibody is identified supporting evidence of immunological risk. The authors would like to thank the recipients who participated in the study and the researchers at the Granulocyte Immunohaematology Research Laboratory for donating blood to perform the GAT and f low-WIFT. We would also like to thank the Coordination for the Improvement of Higher Education Staff [Personnel Coordenação de Aperfeiçoamento de Pessoal de Nível Superior; CAPES] for granting the scholarship and financial aid that made this study possible and Biometrix for the technical support.
Pregnancy-Induced Sensitization in Female Transplant Candidates: HLA-Specific Memory B Cells and Paternal HLA Epitope Mismatch

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Background: Access to kidney transplantation (KT) may be limited by HLA antibodies (HLA-Ab) induced by sensitizing events. Pregnancy is a frequent sensitizing event in female candidates, through which they are exposed to foreign paternal HLA antigens. Consequently, they can generate specific HLA-Ab and memory B cells (mBc), which can be re-stimulated upon antigen reencounter after KT. We aimed to study the existence of mBc able to produce specific HLA-Ab against paternal antigens in female KT candidates sensitised by previous pregnancies, to compare them with HLA-Ab found in their serum and to analyse these HLA-Ab in the context of the molecular HLA mismatch between mother and father.

Methods: We selected 8 HLA sensitised women awaiting KT with at least one successful pregnancy from a single partner, detectable serum HLA-Ab (MFI≥1000) and available paternal DNA for full HLA typing. All women and their partners were typed by next-generation sequencing for HLA–A, B, C, DRB1, DRB3/4/5, DQB1/A1, DPB1. To study mBc, we used peripheral blood mononuclear cells cryopreserved before KT and cultured them with a polyclonal stimulation cocktail consisting of a toll-like receptor agonist and an interleukin for ten days. We examined concentrated culture supernatants (SN) derived from activated mBc, purified IgG and identified HLA-Ab using single antigen beads on Luminex®. Then, we compared the HLA-Ab profiles of SN and serum. We also studied the paternal molecular HLA mismatch with HLAMatchmaker® software.

Results: After 10-day polyclonal stimulation, mBc increased from 29.9% (day 0) to 65.3% (day-10), and antibody-secreting cells (ASC) from 0.1% (day-0) to 29.4% (day-10) (Figure 1). SAB analysis revealed 211 HLA-Ab in serum and 116 in SN: 98/211 (46,5%) HLA-Ab were serum-exclusive (79,6% class I and 20,4% class II) and only 3/116 (2,3%) HLA-Ab were SN-exclusive, all class II. Finally, we found 113/327 (34,6%) HLA-Ab shared by serum and SN: 65/113 (57,5%) class I and 48/113 (42,5%) class II.

Pregnancy-Induced Antibodies (PIA) were present in serum in 6/8 women (21 HLA-Abs: 10 class I, 11 class II) and in 4/8 women in SN (8 HLA-Abs: 2 class I, 6 class II). The HLAMatchmaker analysis showed that those specific HLA-ab were reactive against incompatible paternal epitopes: in 3/6 women for class I & 3/6 women for class II in serum; in 2/4 women for class I & 3/4 women for class II in SN (Table 1).

Conclusion: We describe the study of the memory B cell compartment and the HLA-Ab produced with Luminex technology in KT female candidates with previous pregnancies. We found that the HLA-Ab secreted by memory B cells followed a restricted pattern compared with serum HLA-Ab. The study of paternal HLA molecular mismatch explains many of these HLA-Ab decades after pregnancies. The entire value of this tool for risk stratification in HLA-sensitised patients awaiting TK is currently a matter of study.
Impact of HLA-DQ Mismatch on Renal Transplant Outcomes: A Single-Center Retrospective Cohort Study

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Background: Kidney transplantation remains the treatment of choice among end-stage renal disease patients and little emphasis has been given to the HLA-DQ mismatch determination. The significance in renal outcomes has not been clearly defined. The objective of the study is to determine the association of HLA-DQ mismatches on biopsy proven acute rejection (BPAR), graft function and mortality at 1- and 3- years among living and deceased patients who underwent kidney transplantation.

Methods: This is a retrospective cohort of kidney transplantation performed from 2012 to 2017 in a tertiary renal referral center. Patients were divided into 0-, 1-, 2- HLA DQ mismatches. Continuous and categorical data were analyzed using Mann Whitney-U or Kruskal-Wallis and Chi-square or Fisher's exact tests respectively. Kaplan-Meier Analysis, Log-rank test, Cox-regression and Multiple Linear Regression were used to determine the effect of HLA DQ on acute rejection, graft function and mortality up to 8 years post-transplant.

Results: Among 253 patients included in the study, majority were <50 years old males with non-diabetic nephropathy primarily chronic glomerulopathy and hypertensive nephrosclerosis. 106 patients (42%) have high immunologic profile and majority of patients had living donor. Among the population, 32%, 51% and 17% had 0-, 1-, 2- HLA DQ mismatches respectively. The BPAR among zero HLA-DQ mismatch was 1.25%, 5.12% and 12.23% at 1-, 3- and 5-year post transplant respectively. The BPAR among one HLA-DQ mismatch was 0.78%, 11.14% and 13.73% at 1-, 3- and 5-year post transplant respectively. The BPAR among two HLA-DQ mismatch showed 4.44%, 6.72% and 6.72% at 1-, 3- and 5-year post transplant respectively. The mortality with two HLA-DQ mismatch showed 0%, 0.84% and 2.24% at 1-, 3- and 5-year post transplant respectively while the mortality with one HLA-DQ mismatch showed 0.78%, 11.14% and 13.73% at 1-, 3- and 5-year post transplant respectively. There was no significant difference in BPAR, graft function and mortality by HLA-DQ mismatch when stratified according to immunologic risk. Regression analysis showed no significant association between HLA DQ mismatches and 1- and 3- year BPAR, graft function and mortality.

Conclusion: The study showed that HLA-DQ mismatch was not a significant risk factor for acute rejection, graft function and mortality up to 8 years among kidney transplant recipients.

ABC-Incompatible Liver Transplantation Is a Safe And Effective Intervention for Paediatric Recipients

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Introduction: ABO-incompatible (ABO) Liver transplants in adults are performed infrequently, usually for urgent indications when ABO compatible grafts are unavailable and often require additional desensitisation therapy with mixed outcomes. Several studies have demonstrated comparable rates of graft survival in children less than 2 years of age who receive ABO Liver transplants for non-urgent indications compared to ABO-compatible (ABOc) recipients without the need for desensitisation therapy. These studies have reported mixed outcomes with regards to rejection, biliary complications and rejection. We compared outcomes of children who received an ABO graft with those who received an ABO compatible (ABOc) graft in a single paediatric transplant centre.

Method: A retrospective review of patients aged 0-16 years inclusive who had received ABO Liver transplants from 1986 to 2020 at the Children’s Hospital at Westmead, the Paediatric arm of the Australian National Liver Transplant Unit, Sydney, Australia. Comparison of post-transplant outcomes between first-time ABOc and ABO recipients was made between 2008-2020.

Results: 423 paediatric liver transplants were performed, of which 30 were ABOi. Between 1989 and 1997 6 out of 85 (7.1%) ABOi transplants occurred, at a median age of 7.18. No further ABOi transplants occurred from 1998 to 2007. From 2008 to end of 2020 there were 24 ABOi grafts in children at median age of 0.77. Standard immunosuppression for both groups included tacrolimus (or cyclosporin prior to 1998) and corticosteroids. Basiliximab (interleukin-2 receptor antibody) or a combination of Basiliximab and Rituximab (anti-CD20 antibody) was used more commonly in the ABOi group (63% and 17% respectively) than the ABOc group (29% and 0% respectively). ABOc recipients who received Rituximab were older with a median age of 6.22 (range 4.47-9.01 years) compared to those who didn’t receive Rituximab (median age 0.71, range 0.48-3.64). There was no statistically significant difference in rates of acute cellular rejection (42% vs 34%), antibody mediated rejection (8.2% v 2.4%), sepsis (42% vs 29%), biliary strictures (13% vs 12%) or thrombotic events (13% vs 8.4%) between ABOi and ABOc groups. Graft survival at 5 years post-transplant was 95.8% for ABOi patients and 96.1% for ABOc patients.

Conclusion: ABOi liver transplantation in paediatric patients is a safe and successful intervention when undertaken in the appropriate setting. Our centre has demonstrated comparable complication rates between ABOi and ABOc recipients. The role of conditioning therapy with Basiliximab or Rituximab is uncertain in the young ABOi liver transplant recipients.

Complications ABOi (n=24) ABOc (n=166) p-value
Sepsis 10 (42%) 48 (29%) 0.20
Biliary Stricture 3 (13%) 20 (12%) 0.95
Post-op Thrombotic Events 3 (13%) 14 (8.4%) 0.51
Neurological Events 1 (4.2%) 15 (9.0%) 0.42
PTLD 1 (4.2%) 1 (0.6%) 0.11
ACR 10 (42%) 56 (34%) 0.44
AMR 2 (8.3%) 4 (2.4%) 0.12
Retransplant 1 (4.2%) 15 (9.0%) 0.42
Death 0 (0%) 11 (6.6%) 0.19
Equal Outcome and Fewer Complications With Azathioprine Compared to Mycophenolate in Pediatric First-Time Kidney Transplantation: Should Current Practice Be Re-Evaluated?

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Background: In pediatric kidney transplantation, the immunosuppressive standard practice has shifted over the past two decades. Mycophenolate has largely come to replace azathioprine as the antimetabolite of choice worldwide. The evidence in support of mycophenolate with regards to graft survival in adult kidney transplantation is solid. Yet, there are few studies comparing azathioprine and mycophenolate in pediatric kidney transplantation. The aim of this study was therefore to compare outcome and early complications, using a immunosuppressive protocol including azathioprine or mycophenolate in combination with tacrolimus and prednisolone ± basiliximab induction in pediatric kidney transplantation.

Methods: From 2003 to 2018, 106 pediatric patients (≤16 years) underwent kidney transplantation at Karolinska University Hospital. Patients undergoing re-transplantation or ABO-incompatible transplantation were excluded. In total, 84 first-time kidney recipients receiving standard immunosuppression with tacrolimus and prednisolone ± basiliximab, combined with either mycophenolate or azathioprine were included. Antimetabolite on the day of surgery was used as grouping label in the analysis: 38 patients (45%) received azathioprine (start dose 3 mg/kg), with 0% basiliximab induction (AZA group) and 46 patients (55%) received mycophenolate mofetil (start dose 600 mg/BSA), 11% with basiliximab induction (MMF group).

Results: Mean follow-up (10.4 ± 5.1 yrs) and mean age (7.9 ± 4.9 yrs) did not differ between groups. There was however a difference in dialysis dependence (74% in the MMF group vs 50% in the AZA group, p=0.02) and donor source (67% living donor recipients in the MMF group and 92% in the AZA group, p=0.006). In the MMF group 9 patients were PRA+, but only one patient had PRA > 10%. Patient survival and graft survival were similar across groups (overall 95.1% and 83.5% at 10 yrs). Measured GFR was at 5 yrs similar in the two groups: 51.1±30.6 ml/min/1.73 in the MMF group and 51.3±20.2 ml/min/1.73 in the AZA group (p=0.98). More unscheduled readmissions were observed in the MMF group first year (70% vs 47%, p=0.04), primarily owing to urosepsis (18% vs 0%, p=0.02) and diarrhea (24% vs 6%, p=0.04). No difference was observed between groups regarding rejection episodes (overall 18%) and transplant related infections (CMV/EBV/BKV) during the first year after transplantation.

Conclusion: Based on the experience in adult kidney transplantation, mycophenolate has become the preferred antimetabolite in pediatric kidney transplantation. However, our data suggest that azathioprine is not inferior to mycophenolate in immunologic low-risk pediatric kidney recipients with similar graft survival and potentially fewer complications. However, giving the limitations of this single-center study, further investigations with larger study populations are needed.

Swedish Order of Freemasons.
Results of 922 Pediatric Liver Transplants: Prognostic Factors, Learning Curve and Impact on One-Year Survival

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Objective: The objective of this work is to analyze the impact on one-year survival of pediatric liver transplanted patients during 29 years of the transplantation program at the “Prof. Dr. J.P. Garrahan”.

Materials and Methods: 922 pediatric liver transplants were retrospectively studied, including prognostic factors and the experience curve, and comparing two different stages: Era I (1992-2005) and Era II (2005-2021). Pre, intra and post-transplant variables were defined. A univariate and multivariate logistic regression analysis was performed to evaluate the predictors of mortality and graft loss at one year.

Results: The median weight of patients was 13 kg and the most frequent indication for transplantation was biliary atresia (35%). The living related donor represented 27% of the transplants and those performed with cadaveric liver were: with whole liver (34%), reduced (24%) and split (16%). The overall survival of the patient and the graft at one year was 79.75% and 75.54%, respectively. The risk factors for patient death and graft loss one year after transplantation in the multivariate analysis were: child under 10 kg at the time of transplantation, late retransplantation, liver reduction technique, use of an arterial graft, primary non function and arterial thrombosis. In Era I, there was a greater number of transplants in emergency status, a longer cold ischemia time, a lower number of late retransplants, and a lower delayed closure of the abdominal wall. Overall graft and patient survival at one year improved significantly in Era II from 66.94% to 81.56% (log rank 0.0000) and from 70.88% to 86.30% (log Rank 0.0000), respectively.

Conclusion: The present work demonstrates the evolution in the learning curve over a 29 year period and its relationship with the improvement on early post-transplant survival in a transplant program that takes place in a public hospital in Argentina. The improvements achieved during the second ERA of the program are comparable to international standards and reflect the continuous improvement and experience of an interdisciplinary team.
Outcomes of Single Kidney Transplantation From Pediatric Donors With Acute Kidney Injury Into Pediatric Recipients

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Background: Despite the potential reversibility of acute kidney injury (AKI) lesions, kidneys from AKI pediatric donors are underutilized especially for pediatric recipients. Single kidney transplantation from small pediatric donors to pediatric recipients (PTP) can maximize the number of recipients. The objective of this study is to test whether pediatric recipients transplanted with single AKI pediatric kidneys achieve comparable results to other PTP patients.

Methods: This retrospective cohort study investigated all single kidney transplantation PTP patients between 01/2012 and 12/2020 in a single specialized transplant center. AKI was defined by the pediatric-modified RIFLE criteria. Outcomes were compared using Kaplan-Meier with log-rank test and death-censored graft survival was assessed by multivariable Cox proportional hazard model. The study was approved by the ethics committee of The First Affiliated Hospital, Sun Yat-sen University.

Results: Of all 197 enrolled patients, 60 (30.46%) were transplanted from AKI donors and 137 (69.54%) from non-AKI donors. Patients were followed for a median of 31 months (range, 12-108 months) after transplantation, during which 24 (12.18%) grafts were lost, and 2 (1.02%) patients died of pulmonary infection. Rejection (50%) was the leading cause of graft loss followed by vascular thrombosis (20.83%) and recurrent disease (12.5%). No significant difference was found between the two groups on the incidence of acute rejection over time (P = 0.1597). Primary nonfunction was observed only in one patient from the AKI group. Delayed graft function occurred equally between two groups (16.67% vs. 13.87%, P = 0.61). All groups demonstrated satisfactory graft function, eGFR at 3 years post-transplant was 84.6±22.63, 91.03±33.25mL/min/1.73m² for AKI and non-AKI groups, respectively (P = 0.441). Three-year death-censored graft survival in the AKI group was 83.33%, comparable to the results in the non-AKI group (89.78%, P = 0.226). The adjusted hazard ratio (aHR) for graft loss was similar for recipients of AKI (aHR 1.48, 95% CI 0.65-3.35, P = 0.348) compared with the non-AKI group.

Conclusions: Single kidneys from AKI pediatric donors have at least as good outcomes as non-AKI pediatric donors when transplanted into children. This study provides evidence to support the use of AKI pediatric donors for pediatric single kidney transplantation.

Reference:
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417.5

**Pediatric Liver Transplantation: Twenty-Five-Year Experience at a Single Center**

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**Introduction:** Pediatric liver transplantation (Tx) is a worldwide accepted therapy for those disorders that generate severe and irreversible acute and chronic liver diseases. We aim to report our 25-year experience, performing liver transplantation in children at a single center.

**Material and methods:** Retrospective analysis of patients <18 years old who underwent primary Tx or re-transplant (reTx) of the liver between January 1995 and December 2021 at a single center. Demographic data, time on the waiting list, indication and type of Tx, length of hospital stay, ischemia times, complications, overall graft and patient survivals were analyzed. Survival analysis was also performed comparing 2 different groups, G1: 1995-2008 and G2: 2009-2022. Statistical analysis was performed with SPSS version 25.0.

**Results:** A total of 243 Tx were done, 210 (86%) were primary Tx, 29 were re-Tx and 4 had a 3rd Tx, and 122 (50%) were female. The median age was 33 months (R=1-208), median weight was 13 kg (R=4-74 and z score weight for age -1.07 ± 1.5) and mean height of 100±35 cm (z score height for age -1.7 ± 1.8). Indications for Tx were: 88 (42%) biliary atresia, 33 (16%) cryptogenic acute liver failure, 24 (11%) fulminant viral hepatitis (HAV), 15 (7%) autoimmune hepatitis, 14 (7%) Alagille’s syndrome, 17% others. Re-Tx were performed due to: chronic ductopenic rejection in 12 cases, arterial thrombosis in 7, primary graft dysfunction in 7, biliary complications in 4 and others in 3. The mean time on the waiting list for cadaveric Tx was 81 ± 191 days, mean postTx hospitalization was 28±24 days (12±13 ICU and 15±19 general ward). One hundred fourteen (47%) Tx were performed with living donor; 129 (53%) with cadaveric grafts, of them 61(47%) with partial graft. The mean cold and warm ischemia time were 250±245 minutes and 44±42 minutes respectively: 402±127* and 45±17 minutes for cadaveric donors and 85±67* and 43±12 for living donors of cold and warm ischemia time (* p=0.001). The most frequent surgical complications were: 49 (20%) biliary leaks and 19 strictures, 14(6%) hepatic artery thrombosis (11 early and 3 late), 10 (4%) portal vein (8 thrombosis and 2 stenosis), the remaining 10% were other complications (postoperative bleeding, acute ventral hernia, surgical wound infection, peritonitis); 14 (6%) cases of PTLD. Figure 1 shows patient and graft survival at 1, 5 and 10 years for those who received primary Tx and re-Tx. Figure 2 shows patient’s survival divided in primary Tx and re-Tx.

**Conclusions:** The most frequent cause of primary Tx is biliary atresia, while for re-Tx is chronic rejection. The most frequent early complication was bile leak, and the most frequent late complication was chronic rejection. Long-term survivals exceed the results from other regional and international centers.
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Plasma Level of TGF Beta 1 Is Associated With the Polymorphism rs1800469 of the TGFB1 Gene in Pediatric Liver Recipients

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Introduction: Investigation of new prognostic biomarkers for posttransplant complications is an important issue in today’s transplantology. It has been shown that the blood plasma level of transforming growth factor β1 (TGF-β1) may correlate with graft dysfunction development in pediatric liver recipients. However, it is unknown whether these associations are causal and which factors can determine the cytokine plasma levels. The aim was to access the relations of TGFβ1 blood plasma concentrations before and after liver transplantation (LT) with TGFB1 gene polymorphism in pediatric recipients.

Materials: 136 children (62 boys) with LT; aged from 3 to 192 (median - 11) months and 64 healthy donors (27 men) aged from 27 to 64 (median - 31) years were included in the study. Concentrations of TGFβ1 were measured in blood plasma before, one month and one year after LT by ELISA. The three types (rs1800469, rs1800470 and rs1800471) of single nucleotide polymorphism (SNP) of TGFB1 was studied by TaqMan SNP genotyping assay.

Results: In the liver recipients, the median level of TGF-β1 was 4.17 (1.28-9.29), 6.25 (1.35-15.52) and 7.57 (1.86-13.50) ng/ml before, one month and one year after LT, respectively; frequencies of the SNPs: rs1800469 - 21% AA homozygotes, 35% AG heterozygotes, and 44% GG homozygotes; rs1800470 - 77% AA, 15% AG, 7% GG; rs1800471 - 0% GG, 12% GC, 88% CC. In the donors, the median level of TGF-β1 was 6.65 (3.77-17.77), the SNPs frequencies: rs1800469 - 15% AA, 34% AG and 51% GG; rs1800470 - 85% AA, 15% AG and 0% GG, and rs1800471 - 0% GG, 6% GC, 94% CC. A comparative analysis revealed that the cytokine level in pts. with GG genotype rs1800469 was significantly higher than with AG: 1.87 (0.60-7.25) vs 5.25 (2.86-9.45), p=0.038. Differences in levels of TGF-β1 in pts. or donors with other SNPs were not found.

Conclusion: Higher plasma level of TGF-β1 may be associated with genotype GG rs1800469 TGFB1 in pediatric liver recipients. Further investigation should be carried out to evaluate whether this polymorphism may impact on posttransplant complications.

417.7

One Year Survival Comparison of Deceased Donor Versus Living Donor Hepatic Pediatric Transplantation. Meta-Analysis

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Introduction: The constant improvement of surgical techniques, immunotherapy and intensive care has significantly contributed to the rescue of children with extremely low chances of survival due to terminal liver disease. Probably the most important milestone in this advance was taking a transplant from a living donor. Studies published in recent years show a higher survival rate compared to grafts taken from brain-dead patients.

Purpose: This meta-analysis will attempt to highlight the one-year absolute survival of patients who received a transplant from a living donor (LDLT) compared to those who received a transplant from a brain-dead patient (DDLT).

Materials and methods: The chosen study search formula was used on PubMed and Google Scholar. Cohort or case-control studies that reported one-year survival for both LDLT and DDLT were included. The year of publication was not an exclusion criterion. For the statistical analysis, the MedCalc 19 program was used, where the Forest Plot graphs were also made, as well as a Funnel plot for detecting heterogeneity.

Results: Out of a total of 2585 published articles obtained by applying the search formula, only 13 were classified for qualitative analysis and 11 for quantitative analysis. These 11 studies include 8445 patients under the age of 18 years. Of these, 1842 received a transplant from a living donor (LDLT) and 6651 received a transplant from a brain-dead donor (DDLT). From the point of view of heterogeneity, the Q value is 9.01 with a significance level p=0.53. The level of inconsistency is 0% with a confidence interval (0.00 and 56.6%). Of the 1842 children who received a transplant from a living donor, 1722 survived one year, and of the 6,551 children who received a transplant from a brain-dead donor, 6057 patients survived one year (plot pooled effect odds ratio=1.309 random effects).

Conclusion: In conclusion, for pediatric patients, receiving a transplant from a living donor is superior to that received from a brain-dead donor in terms of survival. Improving the anesthetic techniques, the intensive care techniques along with all the advances in complementary medication will lead to a better degree of survival in the coming years.
Abstracts

417.8

Long-term Results of Kidney Transplantation in Children With Bodyweight Lower Than 10 KG

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Objective: To evaluate long-term results of kidney transplantation comparing low weight (<=10 Kg) to bigger children.

Methods: Unicentric cohort involving children who underwent kidney transplantation. The primary clinical outcomes were the 7 years death-censored graft survival, and the estimated glomerular filtration rate (eGFR) at 1, 3, 5, and 7 years. The main risk variable was weight at transplantation and children were categorized as G1: <= 10Kg and G2 > 10Kg. Covariables were CKD etiology, and kidney donor type (living/deceased). The survival estimates were fit through univariate and multivariable Cox regression models, and the eGFR over time was modeled using multilevel mixed-effects linear regression.

Results: The study involved 451 first kidney transplants in children (53 from G1 and 398 from G2), with a median age of 7.6 (4.0 to 12.5) years, 64% male, 53% CAKUT. G1 had a) more living related donors (28% versus 17%), and b) slightly different CKD etiologies, with more CAKUT (64% versus 52%) and hereditary diseases (23% versus 13%), both results tending towards a significant difference (p=0.06 in both cases). Graft survival at 7 years was 86% (75 to 99) in G1 and 84% (79 to 88) in G2 (p=0.791). The mixed-effects model revealed that both groups had a significant decline in eGFR over time (p<0.001), but with no significant difference (p=0.172) between groups (FIGURE 1). To adjust for the higher proportion of living donors in G1, we analyzed separately the subgroups according to kidney donor type, and these analyses did not change the results of the models.

Conclusions: The main finding of this study is the similar long-term results of kidney transplantation in both groups. This results in a sizeable number of low-weight children should uphold kidney transplantation in small children.

FIGURE 1 – Estimated glomerular filtration rate over time in children according to weight at transplantation.
A Pre-transplant Risk Assessment Tool for Outcome in Pediatric Kidney Transplantation Based on a Dutch Cohort of 1415 Patients

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Background: Donor allocation is an important modifiable factor in pediatric kidney transplantation. A prediction model based on donor characteristics could help optimize graft survival. The aim of this study is to develop a risk assessment tool for graft loss based on essential pre-transplantation characteristics.

Methods: A prospective Dutch registry was used including all transplantation data since 1966. A multivariable binary logistic model with discrete-time event history analysis was used to predict hazard of graft loss. This model was corrected for era of transplantation and course of time after transplantation. Subsequently, a prediction score was calculated based on the B-coefficients. For internal validation a derivation (80%) and validation cohort (20%) were defined. Performance of the model was assessed with area under the curve (AUC) of the receiver operating characteristics curve (ROC), Hosmer-Lemeshow test and calibration plots.

Results: The prediction model was based on 7252 observations after 1415 transplantations in patients [age 1-18] between 1966-2021. 10-years graft survival was 42% for transplantations before 1990 and improved to a current 92%. Over time significantly more living and pre-emptive transplantations and increased donor age were seen (p<0.05). Other variables included in the model were recipient age, number of previous transplantations, number of HLA mismatches, era of transplantation and underlying renal disease. The predictive capacity of this model was very good with AUC scores of 0.81, 0.78, 0.77 and 0.74 after 1, 5, 10 and 20 years respectively (p<0.01). Calibration plots showed excellent fit.

Conclusion: This pediatric pre-transplant risk assessment tool was shown to be highly predictive for graft survival in the Netherlands. This model uses essential variables and could support decision making regarding donor selection and optimizing graft outcome.
The Impact of COVID-19 on Pediatric Organ Donation and Transplantation

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Purpose: The global COVID-19 pandemic has significantly altered delivery of healthcare. Hospital resource utilization has been impacted on multiple levels including solid organ transplantation and overall access to transplant care. In the United States, significant regional variation and decreased living donor transplantation occurred during the initial 6 months of the pandemic. We examined the multi-year impact of COVID-19 on pediatric organ donation and transplantation.

Methods: Pediatric (<18 years of age) organ donation and transplant data was obtained from the Organ Procurement and Transplantation Network (OPTN). Data were reviewed between January 2019 to December 2021 and included pediatric donors after brain death (pDBD), donors after circulatory death (pDCD), living donors (LD), and recipient details including total number of transplants, waitlist deaths, and removals.

Results: Total pediatric transplants performed in 2019, 2020, and 2021 were 1923, 1766, and 1890 (p=0.004) respectively. Organ specific data is outlined in Table 1. In 2019, 2020, and 2021, living donor transplantation accounted for 320, 288, and 311 (p=0.838) cases, while 1579, 1456, and 1552 (p=<0.0001) deceased donor allografts were utilized. There were 171, 176, and 209 pDCD and 746, 684, and 713 pediatric pDBD donors. Living donors across all recipient ages were 7391, 5725, and 6539. Pediatric patients added to all organ waitlists during the study period were 2392, 2337, and 2430. Children removed from the waitlist for all conditions were 2347, 2198, and 2288 with 93, 82, and 76 of those cases due to patient death. There was no statistically significant difference in the proportion of pediatric patients added to the waitlist compared to those removed during 2019-2021 (p=0.505).

Conclusions: Transplant volume transiently decreased in the first six months of the COVID-19 pandemic. However, transplantation rates in children, specifically abdominal organ transplantation, increased to nearly pre-pandemic levels in 2021. Lung transplants were significantly decreased during the study period. Pediatric donation remained relatively steady from 2019-2021. Living donor transplantation in children was significantly impacted in 2020. Waitlist additions/removals remained consistent throughout the study period.

Table 1:

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<td>Liver</td>
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<td>66</td>
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<td>58/86</td>
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* p-value reflective of the proportion of overall pediatric transplants in 2019, 2020, or 2021 over the sum of all pediatric transplants occurring during those years.

417.10
Influence of Migration Status on Practice and Clinical Course of Pediatric Kidney Transplantation
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Objectives: to investigate the incidence trend of transplanted immigrant children and to analyze kidney transplant (KTx) practice and outcome for immigrant compared to native children.

Methods: We performed a retrospective study: i. to analyze the percentage trend of “foreign patients” (FP) (children with one/both parents born in non-Western European countries) aged ≤21 years, transplanted in the period 2002-2021 at our Center; ii. to compare data of FP and “domestic patients” (DP) during the period 2017-2021.

Results: The percentage of FP was 22.3% and 34.6% (p:0.04) in the decades 2002-2011 and 2012-2021 respectively. Baseline and transplantation characteristics of patients in the period 2017-2021 are summarized in Table 1.

Compared to DP, FP receive less pre-emptive and living donor (LD) KTx and spend more time on dialysis before KTx. Moreover, Kaplan-Meier survival analysis was used to assess the 5-year KTx survival (patients censored at acute rejection episodes [ARE]) and showed a significant increased risk of ARE in FP compared to DP (7 vs 1 events, p < 0.003). The first ARE occurred after a period of 3.8 months (IQR 3.1-7.2) and 26.1 months in FP and DP patients respectively. We also found a significant difference in HLA mismatch with a higher mean value in FP population.

Conclusion: Our study confirms the progressive increase of FP in recent years in Italy. In line with other studies in Europe, we found disparities in practice and outcomes of KTx in FP; that can be attributed to cultural factors and language difficulties, even if immunological and genetic factors, such as different pharmacokinetic profile, should be analyzed. While waiting to better understand the mechanisms behind this phenomenon, it can be useful to build a multidisciplinary network and ad hoc initiatives around FP, in order to support these patients and their family to improve their outcome.

Table 1: Baseline and transplantation characteristics

<table>
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<tr>
<th>Characteristic</th>
<th>Total (n=75)</th>
<th>Domestic patients (n=50)</th>
<th>Foreign patients (n=25)</th>
<th>p</th>
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<td>Age at transplantation (years)</td>
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<td>11.4 (6.4)</td>
<td>12.7 (5.5)</td>
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<td>Sex, female, n (%)</td>
<td>20 (26.7)</td>
<td>14 (28.0)</td>
<td>6 (24.0)</td>
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<td>Primary cause of ESRD, n (%)</td>
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<td>23 (46.0)</td>
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<td>11 (22.0)</td>
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<td>3 (6.0)</td>
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<tr>
<td>Other glomerular disease</td>
<td>5 (6.7)</td>
<td>4 (8.0)</td>
<td>1 (4.0)</td>
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<tr>
<td>CRF</td>
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<td>Hereditary nephropathy</td>
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<td>Kidney failure</td>
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<td>6 (12.0)</td>
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<tr>
<td>Others</td>
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<td>1 (2.0)</td>
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<tr>
<td>Follow-up time (months)</td>
<td>27.3 (14.6-47.0)</td>
<td>32.0 (17.3-69.2)</td>
<td>18.7 (6.4-69.9)</td>
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<td>Pre-emptive KTx, n (%)</td>
<td>25 (33.3)</td>
<td>22 (44.0)</td>
<td>3 (12.0)</td>
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<td>LDL KTx, n (%)</td>
<td>19 (25.3)</td>
<td>18 (36.0)</td>
<td>1 (4.0)</td>
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<td>Time on dialysis before KTx (months)</td>
<td>10.9 (2.23.7)</td>
<td>3.7 (0.5-15.0)</td>
<td>16.7 (10.0-30.0)</td>
<td>0.800*</td>
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<td>HLA mismatches (A, B, DR)</td>
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<td>3.4 (1.0)</td>
<td>0.92*</td>
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<tr>
<td>&gt; 1 mismatch on DR, n (%)</td>
<td>6.0 (0.0)</td>
<td>4.0 (0.0)</td>
<td>2.0 (0.0)</td>
<td>ns</td>
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</tbody>
</table>

*Data are presented as median and interquartile range
**Follow-up time was calculated per patient in months from the KTs date until the first ARE or KTx failure or the last follow-up visit
***Data are presented as mean ± standard deviation
****Mann-Whitney U-test
*****Chi-square test
†††Test for unscored data
417.12

**Eculizumab Therapy for Late Antibody-Mediated Rejection in Pediatric Kidney Transplant Patients**

Meraj Alam Siddiqui¹, Esra Baskin¹, Feza Yarbug Karakayali², Atilla Gemici³, Kaan Guillieroglú¹, Aysun Çalik Yilmaz⁴, Gokhan Moray², Mehmet Haberal².

¹Department of Pediatric Nephrology, Baskent University, Ankara, Turkey; ²Department of General Surgery, Division of Transplantation, Baskent University, Ankara, Turkey.

**Background:** Late antibody-mediated rejection (ABMR) triggered by donor-specific antibodies (DSA) is a major clinical challenge and a leading cause of kidney allograft failure. Effective treatment options for late ABMRs are limited in renal transplant recipients. Eculizumab targets complement protein C5, preventing its conversion to C5a and C5b, thereby inhibiting the formation of the membrane attack complex and complement mediated injury (Figure 1). Here, we report two pediatric cases of severe late ABMR, resistant to conventional immunosuppressive therapy who were successfully treated with eculizumab.

**Methods:** Two patients who fulfilled late ABMR diagnostic criteria (positive DSA, elevated means fluorescence index (MFI) value, acute and/or chronic morphological lesions in the microvasculature and abnormal kidney function test) were included in this study. Both patients' panel-reactive antibody test results were negative.

**Case Reports:**

**Case 1:** An unsensitized 12-year-old male patient presented with chronic renal disease secondary to vesicoureteral reflux (VUR) who underwent related-living donor kidney transplantation 2 years ago. Six months after transplantation, patient presented with abnormal kidney function. His donor-specific antibody (DSA) was positive, means fluorescence index (MFI) value was 13000 and renal biopsy showed a strong complement C4d positivity in the peritubular capillaries. Despite conventional immunosuppressive regimen including steroid boluses, plasmapheresis, intravenous immunoglobulin and rituximab, signs of rejection persisted. Patient was treated with 2 doses of eculizumab. Following the eculizumab treatment, MFI value dropped below 3000. Serum creatinine level dropped from 3.8 mg/dL to 1.5 mg/dL.

**Case 2:** An unsensitized 16-year-old male patient with kidney failure secondary to posterior urethral valve (PUV) underwent related-living donor kidney transplantation 4 years ago. Six months after transplantation, patient presented with abnormal kidney function. His donor-specific antibody (DSA) was positive, means fluorescence index (MFI) value was 11000 and renal biopsy showed a strong complement C4d positivity in the peritubular capillaries. Despite an aggressive conventional immunosuppressive regimen, signs of rejection persisted. Patient was also treated with 2 doses of eculizumab. Following eculizumab treatment, MFI value dropped below 2000 and serum creatinine level decreased from 2.1 mg/dL to 1.01 mg/dL.

**Conclusion:** In both cases, eculizumab therapy effectively reduced the markers of late antibody-mediated rejection and improved kidney function. An early initiation of eculizumab treatment as primary therapy along with the conventional immunosuppressive regimen is safe and effective for late antibody mediated graft rejection in kidney transplant patients.

<table>
<thead>
<tr>
<th>Variables</th>
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<td>Primary disease</td>
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VUR, Vesicoureteral reflux; PUV, Posterior urethral valve; MMF, Mycophenolate mofetil; IVIG, Intravenous immunoglobulin
Successful Transplantation From Selected SARS-CoV-2 RNA Positive Deceased Donors

Ines Ushiro-Lumb1, Susanna Madden1, Gavin Pettigrew1, Douglas Thorburn1, Chris Callaghan1, Derek Manas1

1Organ and Tissue Donation and Transplantation, National Health Service Blood and Transplant, London, United Kingdom.

Introduction: In the UK, the SARS-CoV-2 status of deceased donors is assessed by specific questionnaire and by universal Nucleic Acid Test (NAT) for SARS-CoV-2 RNA in nose and throat swabS (NTS) and endotracheal aspirates (ETA). Initially, only asymptomatic and NAT-negative donors were accepted. Improved understanding of the relationship of SARS-CoV-2 replication to viral RNA detection as well as a more detailed testing approach have enabled consideration of NAT-positive donors.

Methods: Donor information and detailed SARS-CoV-2 RNA screening results were collected in real-time. SARS-CoV-2 NAT positivity triggered repeat sampling for the clarification of significance. Laboratory-proven diagnosis of SARS-CoV-2 infection in deceased donors or recipients of solid organs in England were captured by data linkage between the organ transplant registry and the National laboratory reporting system. Recipient infection within 14 days from organ transplantation was reviewed for the possibility of donor-transmitted infection.

Results: Between 1st March 2020 and 9th February 2022, 3537 potential donors were assessed in the UK. Thirty-seven tested NAT positive during donor assessment, with 17 not proceeding to donation due to the result (15) or due to other reasons (2). Of the remaining 20, the majority had a result profile indicating previous resolved infection, with detection of residual viral RNA; in the absence of evidence of previous infection some of the very weakly reactive NAT results might have been due to false positivity. Two donors had results compatible with current but resolving asymptomatic infection. Organs from these 20 donors were offered for transplantation, resulting in 57 organ transplants into 53 recipients (3 heart, 14 liver, 3 pancreas, 31 kidney). Six lungs were transplanted from donors with NAT negative ETA and whose positive NTS results were at the limit of assay detection and not repeatable upon re-sampling. No donor-transmission of virus has been identified, with good transplant outcomes achieved.

Conclusion: SARS-CoV-2 RNA positivity should be verified and interpreted in conjunction with clinical, epidemiological and virological information. In an asymptomatic individual, other than a current infection, positivity could also be due to previous, resolved infection with detection of residual viral RNA; current, resolving infection; or a false-positive result. This enables consideration of organs that would otherwise be deemed unsafe for transplantation. Our preliminary results suggest that organs other than lungs can be safely transplanted, without SARS-CoV-2 transmission, from selected NAT-positive deceased donors in whom SARS-CoV-2 infection is considered either historical or non-evolving.

Early Experience of Solid Organs Transplantation From COVID-19 Positive Donors in a Single Institute

Jorge Sanchez-Garcia1, Philippe Paci1, Camron Dovalina2, Abigail Ha1, Becca Welch2, Ivan Zendejas1, Alan G Contreras1,3, Shiro Fujita1,3, Manuel I Rodriguez-Davalos1,3, Diane Alonso1

1Liver Transplant Service, Intermountain Medical Center, Murray, UT, United States; 2Organ Recovery Services, Donor Connect, Murray, UT, United States; 3Liver Transplant Service, Primary Children's Hospital - Intermountain Healthcare, Salt Lake City, UT, United States.

Introduction: COVID-19 pandemic impacted organ transplantation in the United States. Organs from COVID-19 positive donors had a higher post-procurement discard rate when compared to COVID-19 negative donors. The aim to this study is to report the experience in utilization organs from COVID-19 positive donors.

Methods: Retrospective review of all donors with history of COVID-19 positive from March 2021 and December 2021 in a single institution. Donors were classified in two groups: early window (<10 days of their first positive test) and late window (>21 days of their first positive test). Primary endpoint was pulmonary complications (i.e., pulmonary embolism, and pneumonia) in the recipients within 30 days after transplantation. Secondary endpoints were graft and patient survival.

Results: A total of 50 organs from COVID-19 positive donors were recovered (34 kidneys, 11 livers and 5 hearts) in the region. Of these, 17 organs (13 kidney and 4 livers) from 10 COVID-19 positive donors were allocated to our institution. Seven donors were male (70%), median age was 29 (IQR 22-55) years old. Five grafts were from donation after circulatory death (DCD, 50%), with a median warm ischemia time of 19 minutes (IQR: 19-20). Four donors (40%) were hospitalized due to COVID-19 infection, while the remainder tested incidentally positive during the donor workup. The median time of first COVID-19 positive test to procurement date was 5 (IQR 3.3-24.8) days. Six donors were classified as early window and four donors were classified as late window. Of the former, three remained with a positive COVID PCR test with cycle threshold values ranging from 35-38.1 at the time of procurement. Donors (25 vs 60 years, p=0.068) and recipients (44 vs 65 years, p=0.008) were younger, and a lower rate of DCD (1 vs 4, p=0.053) was observed in the early window group. Peak creatinine (1.2 vs 1, p=0.7) and total bilirubin (0.7 vs 1, p=0.7) were similar between groups, and graft terminal median creatinine and median total bilirubin was 0.9 (IQR 0.8-1) mg/dL and 0.4 (IQR 0.3-0.6) mg/dL, respectively for both groups. Overall, 13/17 recipients were males, with a median age of 50 years old (IQR: 43-63). Median waitlist times were 1165 days (IQR: 572-1520), and 342.5 days (IQR: 284-398) for kidney and liver recipients, respectively. The length of stay was 4 (IQR 3-4) and 9 days (IQR 8-11) for kidney and liver recipients with no pulmonary complications recorded. Median follow up time was 3 (IQR 2-6) months, and no graft loss or patient death was recorded.

Conclusion: COVID-19 positive donors in solid organ transplantation appear to have minimal risk for post-transplant complications in the short-term. Donors having a COVID-19 positive test with a high threshold can be recommended depending on the recipient’s risk for wait list mortality.
The Use of mTOR Inhibitors Is Associated With Reduced Mortality Among Kidney Transplant Patients Developing COVID-19

Lúcio Requião-Moura1,2,6, Luís Gustavo Modelli de Andrade3,6, Tainá V Sandes-Freitas1,5,6, Marina P Cristelli2, Laila A Viana2, Mônica R Nakamura2, Valter D Garcia6, Roberto C Manfro6, Denise R Simão6, Ricardo Augusto M Barros Almeida6, Gustavo F Ferreira6, Kellen Micheline A Henrique Costa6, Paula R Lima6, Alvaro Pacheco-Silva6, Ida Maria M Fernandes Charpiot6, Luciane M Deboni6, Carlos Alberto C Calazans6, Reinaldo B Oriá6, Hélio Tedesco-Silva1,2,6, José Medina-Pestana1,2,6.

1Nephrology Division, Universidade Federal de São Paulo, São Paulo, Brazil; 2Hospital do Rim, Fundação Oswaldo Ramos, São Paulo, Brazil; 3Department of Internal Medicine, Universidade Estadual Paulista-UNESP, Botucatu, Brazil; 4Programa de Pós-Graduação em Ciências Médicas, Universidade Federal do Ceará, Fortaleza, Brazil; 5Hospital Universitário Walter Cantídio, Universidade Federal do Ceará, Fortaleza, Brazil; 6COVID-19-KT Brazil Study Group, Brazil;

Abstracts

420.3
The Use of mTOR Inhibitors Is Associated With Reduced Mortality Among Kidney Transplant Patients Developing COVID-19

Lúcio Requião-Moura1,2,6, Luís Gustavo Modelli de Andrade3,6, Tainá V Sandes-Freitas1,5,6, Marina P Cristelli2, Laila A Viana2, Mônica R Nakamura2, Valter D Garcia6, Roberto C Manfro6, Denise R Simão6, Ricardo Augusto M Barros Almeida6, Gustavo F Ferreira6, Kellen Micheline A Henrique Costa6, Paula R Lima6, Alvaro Pacheco-Silva6, Ida Maria M Fernandes Charpiot6, Luciane M Deboni6, Carlos Alberto C Calazans6, Reinaldo B Oriá6, Hélio Tedesco-Silva1,2,6, José Medina-Pestana1,2,6.

1Nephrology Division, Universidade Federal de São Paulo, São Paulo, Brazil; 2Hospital do Rim, Fundação Oswaldo Ramos, São Paulo, Brazil; 3Department of Internal Medicine, Universidade Estadual Paulista-UNESP, Botucatu, Brazil; 4Programa de Pós-Graduação em Ciências Médicas, Universidade Federal do Ceará, Fortaleza, Brazil; 5Hospital Universitário Walter Cantídio, Universidade Federal do Ceará, Fortaleza, Brazil; 6COVID-19-KT Brazil Study Group, Brazil;

Background: The chronic use of immunosuppressive drugs is a key risk factor of death due to COVID-19 in kidney transplant recipients (KTRs), although no evident association between the class of immunosuppressive and outcomes has been observed. Thus, we aimed to compare COVID-19-associated outcomes among KTRs receiving three different immunosuppressive maintenance regimens.

Methods: This study included data from 1,833 KTRs with COVID-19 diagnosed between Mar/20 and Apr/21 extracted from the national registry prior to immunization. All patients were taking calcineurin inhibitor (CNI) associated with mycophenolate (MPA, n=1,258), azathioprine (AZA, n=389) or mTOR inhibitors (mTORi, n=186). Outcomes within 30 and 90 days were assessed. Patient survival was estimated by Kaplan-Meier and the multivariable analysis was provided by center-adjusted Cox regression models.

Results: The overall hospitalization rate was 65.5% and was lower among patients in the CNI-AZA group compared with CNI-MPA (45.6% vs. 66.7%, p<0.001) and CNI-mTORi (45.6% vs. 61.1%, p=0.001, figure 3). The overall admission rate to the ICU was 32.3%, higher in the CNI-MPA than CNI-AZA (35.7% vs. 25.8%, p<0.001) and CNI-mTORi (35.7% vs. 22.6%, p<0.001). Last, 23.5% of the patients required mechanical ventilation, a higher proportion in the CNI-MPA group compared with CNI-AZA (26.8% vs. 17.8%, p<0.001) and to CNI-mTORi (26.8% vs. 13.4%, p<0.001). Compared with patients receiving MPA, the 30-day (79.9% vs. 87.9% vs. 89.2%, p<0.0001) and 90-day (75% vs. 83.5% vs. 88.2%, p<0.0001) unadjusted patient survival was higher in those receiving AZA or mTORi, respectively.

Using adjusted multivariable Cox regression, compared with patients receiving AZA, the use of MPA was associated with a higher risk of death within 30 days (aHR=1.70; 95%CI= 1.21–2.40; p=0.003), which was not observed in patients using mTORi (aHR=0.78; 95%CI= 0.45-1.35; p=0.365). At 90 days, while higher risk of death was confirmed in patients receiving MPA (aHR=1.46; 95%CI= 1.09-1.98; p=0.013), a reduced risk was observed in patients receiving mTORi (aHR= 0.59; 95%CI= 0.35-0.97; p=0.04) compared with AZA.

Conclusion: This national cohort data suggest that in kidney transplant recipients receiving CNI and diagnosed with COVID-19, the use of MPA was associated with higher while mTORi use was associated with lower risk of death.
420.4

Single Center Clinical Outcomes of 112 Kidney Transplant Recipients of SARS-CoV-2 Positive and Negative Deceased Donors

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1Kidney Medicine, Cleveland Clinic, Cleveland, OH, United States; 2Infectious Disease, Cleveland Clinic, Cleveland, OH, United States; 3Urology, Cleveland Clinic, Cleveland, OH, United States; 4Qualitative Health Sciences, Cleveland Clinic, Cleveland, OH, United States.

Introduction: Kidneys from deceased donors with SARS-CoV-2 infection during donor evaluation have not been accepted by most transplant centers due to concerns for productive COVID-19 infection and organ injury from COVID-related complications or viral transmission leading to de novo recipient infection. Our transplant center developed protocols to accept such kidneys. We aimed to compare clinical outcomes of kidney transplants (KT) from deceased donors with and without SARS-CoV-2 infection (CoVDpos and CoVDneg, respectively).

Methods: We retrospectively reviewed donor and recipient data and key clinical outcomes for all CoVDpos KT recipients performed at our center between 02/01/2021 and 01/31/2022, and compared such data to all consecutive CoVDneg KT recipients performed during the same period. Donor organ acceptance was pre-established by a protocol developed specifically to select CoV positive deceased donors. No COVID-directed therapies were provided to CoVDpos KT recipients. Standard of care induction therapy (lymphocyte-depleting agents) and a CNI-based maintenance regimen was used for all transplant recipients independent of donor type. Recipient vaccination prior to transplantation was not required in early 2021 but mandated after November 2021.

Results: There were 221 KTIs, including 112 (51%) KT recipients (from a total of 63 CoVDpos deceased donors) and 109 KTIs from CoVD neg deceased donors. Median time from positive SARS-CoV-2 PCR test to donation was 16 days with a mean PCR threshold cycle of 30. Mean KDPI was 36+/−21 vs 45%+/−24 for the CoVDpos vs CoVDneg, respectively. DCD donors were more common in CoVDpos when compared to CoVDneg KTIs (71% vs 47%, p <0.001). Of the 63 CoVDpos donors, 30 (48%) died of COVID complications, mostly hypoxic respiratory failure, with 5 on VV ECMO. Pretransplant vaccination was 96.5% of CoVDpos recipients and 87.2% of CoVDneg KT recipients. Having a CoVDpos kidney transplant was not associated with increased incidence of DGF (15.2% vs 22%, p=NS), KT recipients of CoVDpos organs had similar eGFR at last follow up when compared to recipients of CoVDneg kidneys (47+/−20 vs 2+/−23 ml/min/1.73m2, p=NS), In a multivariable analysis, only recipient age, recipient BMI and DCD were independently associated with post-transplant GFR, while donor Covid-19 infection status was not found to be statistically significant. There was 1 patient death (from progressive pre-existent interstitial lung disease in the absence of SARS-CoV-2 detection from lower airway by BAL) 4 months post-KT, compared to 4 patient deaths in the CoVDneg group, all from non-COVID-19 related illnesses. No kidney transplant recipients developed COVID-19 immediately post-transplant.

Conclusions: Kidney transplant outcomes including graft function was similar in recipients of CoVDpos to those of CoVDnegs out 12 months post-transplant. There was no clinical evidence of SARS-CoV-2 transmission demonstrating the safety of this protocolized approach. Careful utilization of kidneys from CoVDpos donors could minimize unnecessary discard of organs.

420.5

Safety of Accepting Kidneys From Deceased Kidney Donors Who Tested Positive for COVID-19 Virus

Hatem Ali1, Mahmoud Mohammed2, David Briggs2, Nithya Krishnan1.
1Renal department, University Hospitals of Coventry and Warwickshire, Coventry, United Kingdom; 2NHSBT, Birmingham, United Kingdom; 3University Hospitals of Mississippi, Mississippi, United States.

Introduction: Our modern world is facing extraordinary circumstances while passing through a serious pandemic caused by the novel coronavirus (COVID-19) which may lead to multi-organ system failure & death. COVID-19 deaths may provide a potential source for kidneys available for transplantation. In our study, we are discussing the safety of receiving kidneys from donors who tested positive for the novel coronavirus.

Methodology: All renal transplant recipients registered in UNOS database who had their transplants between 1st of March 2020 and 1st of June 2021 were retrospectively reviewed. Patients who received kidney transplants from a deceased donor with positive PCR of COVID-19 test were included in our study. Patients were followed up till 1st of July 2021. Data about recipient factors (age, sex, ethnicity, diabetes, date of renal transplant), transplant factors (type of induction therapy, maintenance immunosuppressive therapy, delayed graft functions, early post-operative rejection episodes, HLA mismatch, PRA level, cold ischemia time) and donor factors (age, sex, ethnicity, diabetes, hypertension, date of COVID-19 test, type of COVID-19 test) were collected. Outcome measured were post-transplant hospitalisation, acute rejection, delayed graft function, patient and graft survival till the end of the follow-up.

Results: 86 transplant patients received kidneys from deceased donors who tested positive for COVID-19 infection using PCR test. 60 patients received kidneys from deceased patients who tested positive for COVID-19 within 30 days pre-transplant. 26 patients received kidneys from deceased patients who tested positive for COVID-19 between 30 to 90 days pre-transplant. Number of post-transplant hospitalisation and acute rejection episodes were nil. 19.76% of the patients had delayed graft functions. Graft loss occurred in one patient due to graft vein thrombosis. Patient survival was 100%.

Conclusion: Receiving kidneys from deceased donors who tested positive for COVID-19 infection seems safe and does not affect hospitalisation, acute rejection rates, graft or patient survival. Longer follow-up is needed to confirm our results.

N.B: We presented similar abstract earlier in ESOT 2021. In our previous abstract, the number of patients included was very small. Only 5 patients. In the current abstract, we are presenting an updated results with much larger number of patients (85 patients).
Transplantation of Organs From SARS-CoV-2-Positive Donors To Uninfected (Non-lung) Solid Organ Transplant Recipients Has Not Resulted in Significant SARS-CoV-2 Related Morbidity Or Mortality

Wasim Dar1,2,4, Jason Wade1, Ayaz Ali2,3,4, Joseph A. Radojevic2,3,5, Jonathan A. Hammond2,3,4, Jason Gluck2,3,5, Andrew D. Feingold2,3,5, Abhishek Jaishwal2,3,5, Zeynep Ebcioglu2,5, Michael Einstein2,5, Glyn Morgan1,2,4, Bishoy Emmanuel1,2,4, Xiaoyi Ye2,5, Joseph Singh1,2,4, Elizabeth Richardson1,2,5, Joseph Tremaglio2,5, Oscar Serrano1,2,5, Colin Swales2,5, Rebecca Kent2,5, Eva U. Sotil2,5, Rebecca Kent2,5, Elizabeth Richardson1,2,5, Joseph Tremaglio2,5, Faiqa Cheema2,5, 1Surgery, Hartford Hospital, Hartford, CT, United States; 2Transplant and Comprehensive Liver Center, Hartford Hospital, Hartford, CT, United States; 3Center for Advanced Heart Failure and Pulmonary Vascular Disease, Hartford Hospital, Hartford, CT, United States; 4Surgery, University of Connecticut School of Medicine, Farmington, CT, United States; 5Medicine, University of Connecticut School of Medicine, Farmington, CT, United States.

Introduction: The SARS-CoV-2 pandemic has conferred significant morbidity and mortality across the globe, especially for solid organ transplant (SOT) recipients. This has led to reluctance of using organs from SARS-CoV-2 infected donors due to concerns of disease transmission. However, this must be offset with an increase in wait list mortality. We sought to evaluate the use of organs from SARS-CoV-2 donors into (non-Lung) Solid Organ Transplant Recipients in a prospective fashion.

Methods: We evaluated the use of organs from SARS-CoV-2 donors between 6/17/2021 to 2/24/2022. 18 patients were transplanted with SARS-CoV-2-positive donor (COVID+) organs: 3 heart, 4 liver, and 11 kidney recipients. SOT recipients were tested for presence of SARS-CoV-2 by RT-PCR prior to and after their operations. Induction immunosuppression was standard and not altered from protocol. Postoperatively, recipients were kept in modified droplet precautions and received post-exposure treatment recommended by Transplant Infectious Disease. Treatment regimens included remdesivir and monoclonal antibodies directed against SARS-CoV-2 (Figure 1). Perioperative and post discharge care was administered by a multidisciplinary care team with no significant alterations in care protocols.

Results: SOT recipients of COVID+ organs at our institution have not experienced any significant morbidity or mortality from SARS-CoV-2. All patients are alive at current follow up with excellent allograft function with a median follow up for heart, liver, and kidney recipients of 255, 67, and 86 days respectively. All patients were vaccinated except for one liver patient who was status 1A due to fulminant acute liver failure. 13/18 patients had post-operative nasopharyngeal swabbing for RT-PCR based viral testing and two tested positive for SARS-CoV-2 at POD #8. Neither patient experienced clinical symptoms of disease. Use of SARS-CoV-2 did not appear to increase inpatient hospital stay. Median LOS for heart, liver, and kidney recipients was 40, 12.3, and 7.4 days respectively. Neither pre-transplant vaccination, use of COVID+ organs, nor post exposure prophylaxis resulted in increased risk of immunologic complications as only one recipient (heart) has experienced an acute cellular rejection episode to date.

Conclusion: Our experience indicates that COVID+ organs can be utilized successfully. The decision to use these organs was based on organ quality, individual patient need at the time the organ offer was made and whether a potential similar quality, COVID negative organ would be available to the patient in the near future. As evidenced by our data, successful use of COVID+ organs is dependent on multidisciplinary wait list and perioperative management to ensure appropriate donor:recipient selection and mitigation of transmission risk with use of post-exposure prophylaxis.
Six Scenarios That Trigger Organ Donation Conversations With NOK: One OPO’s Experience


Introduction: Increased authorization rates are critical to addressing the organ donor shortage. Initiating the authorization conversation with next-of-kin (NOK) at the right time to preserve the option for donation is an important skill in obtaining the best possible outcome.

Method: Authorization and donation outcomes were analyzed retrospectively for 3,617 organ donation conversations with the NOK of medically suitable, vent-dependent patients referred to the OPO between 1/1/2019 and 12/31/2021. OPO transplant coordinators (TC) received specialized training in addition to pro-active, hands-on coaching from a senior administrator on-call to collaborate with hospital care teams in determining the best time to initiate a donation discussion with NOK. Donation conversations were initiated before pronouncement of brain death to preserve the option of donation in cases where there was 1. a decision to withdraw life sustaining therapies, 2. a decision to limit life sustaining therapies, 3. early mention of donation by the hospital care team, 4. family initiation of the conversation, 5. when the patient was hemodynamically unstable or 6. when the OPO determined that the NOK was ready based on their understanding of their loved one’s prognosis.

Results: The overall authorization rate over the 3-year study period was 58% and the donation rate was 55%. When NOK initiated the donation conversation, authorization and donation rates were the highest at 90% and 86% respectively. When the donation conversation was initiated based on the NOK’s understanding of the non-survivable nature of their loved one’s injury, authorization and donation rates were 67% and 65% respectively. When the donation conversation was initiated after a decision to withdraw life-sustaining therapies, authorization and donation rates were the lowest at 45% and 42% respectively.

Conclusion: Obtaining authorization for organ donation is a process, not an event. Approaching families at the right time in order to preserve the option of organ donation that might otherwise be lost is critical. OPOs should collaborate with hospital care teams to provide families with end-of-life care that supports their understanding of the non-recoverable nature of their loved one’s injury. OPOs should educate hospital care teams regarding the importance of early referral and collaboration with the OPO before discussing withdrawal of life-sustaining therapies with families because NOK are far less likely to authorize donation if approached after a withdrawal decision has been made.

One Organ Procurement Organization’s 26-Year Experience With Uncontrolled DCD Donation


Introduction: Uncontrolled DCD donation is an underutilized method of procurement in the U.S., with 44% of all uncontrolled DCD donors to date being procured by one of 57 OPOs. The purpose of this study is to demonstrate that uncontrolled DCD organ donation can lead to the successful retrieval of transplantable organs and to evaluate kidney and liver transplant outcomes for recipients of organs from uncontrolled DCD donors.

Methods: This is a retrospective single OPO, multi-center study. As a standard of practice the OPO routinely pursued uncontrolled DCD donors in the setting of hemodynamic instability and/or sudden cardiac arrest. The aggressive pursuit of these types of donors required the OPO to establish the following: an organizational expectation, training, active AOC oversight, a system to rapidly deploy resources, a communication plan with care-giving team members, and 24-hour organ preservation and surgical recovery support. Graft survival was determined by the Kaplan-Meier method. PNF, age, kidney PNF and DGF were further evaluated by donor Maastricht category.

Results: Between 1996 and 2021, 334 kidneys, 15 livers, 2 pancreata and 1 lung was transplanted from 262 uncontrolled DCD donors. The mean donor age was 33 years (r = 0.5 – 76, sd=15). The median warm ischemic time was 44 minutes (IQR = 22 - 83). Kidney graft survival was 84% at 6 months, 78% at 1 year and 71% at 3 years. Of the 15 livers transplanted, 9 grafts implanted prior to 2010 failed within 3 months, but all 3 of the grafts implanted in 2021 are functioning at 6 months post-transplant. Two of the liver grafts are functioning at 12 years post-transplant and one is functioning at 19 years post-transplant. The lung graft is functioning at 8 years post-transplant.

Conclusions: Uncontrolled DCDs provide acceptable kidney graft survival outcomes and represent a pool of organs that should be pursued for transplantation. OPOs should develop protocols to effectively recover organs from uncontrolled DCDs, particularly in light of promising new advancements in organ preservation.

<table>
<thead>
<tr>
<th># Donors</th>
<th>Mean Age</th>
<th>Median WIT [IQR] (min)</th>
<th>PNF Rate</th>
<th>DGF Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC II</td>
<td>116</td>
<td>31</td>
<td>49 [29-100]</td>
<td>3.6%</td>
</tr>
<tr>
<td>MC IV</td>
<td>57</td>
<td>40</td>
<td>25 [13-46]</td>
<td>1.5%</td>
</tr>
<tr>
<td>MC V</td>
<td>89</td>
<td>28</td>
<td>49 [24-83]</td>
<td>4.7%</td>
</tr>
<tr>
<td>All</td>
<td>262</td>
<td>33</td>
<td>44 [22-83]</td>
<td>4.2%</td>
</tr>
</tbody>
</table>
**ASCENT (Allocation System Changes for Equity in Kidney Transplantation) Implementation of Randomized Effectiveness Study Increased Access to Kidney Transplant Waitlist for Black Patients on Dialysis**

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**Background:** Black vs. white patients have longer time on dialysis and lower rates of kidney transplant access. The U.S. kidney allocation system (KAS) was overhauled in December 2014; however, no formal education was provided to dialysis facilities about the policy and its implications, including how patients with longer time on dialysis could get transplanted faster under the new system.

**Methods:** The ASCENT study was a cluster-randomized, pragmatic, multi-level (provider and patient), multicomponent educational and quality improvement effectiveness-implementation intervention intended to provide education and awareness of the KAS policy change among U.S. dialysis facilities with low waitlisting. A total of 655 U.S. dialysis facilities (>20,000 patients) were randomized. Intervention activities included an educational webinar for medical directors, a staff educational video describing KAS, a transplant performance audit and feedback report detailing the facility-specific impact of KAS, and a patient educational video; the control group received a brochure. Co-primary outcomes of the trial included dialysis facility-level 1-year waitlisting and racial disparity in waitlisting. Generalized linear models reported effects among incident and prevalent patients, adjusting for time trends and clustering of patients within facilities.

**Results:** Similar to national trends, the overall mean proportion of patients waitlisted in a facility declined 1 year after the intervention among incident patients (Figure 1, Panel A, left). However, the proportion of patients waitlisted declined for white ESKD patients in the intervention groups but increased for Black ESKD patients in both the incident (Figure 1, Panel A) and prevalent (Figure 1, Panel B) populations. Mean waitlisting significantly (p<0.05) increased among prevalent Black ESKD patients in the intervention group (baseline waitlisting: 2.52% (2.43, 2.61); follow-up: 2.76% (2.69, 2.87) while it declined among Black patients in the control group (baseline waitlisting: 2.71% (2.62, 2.80); follow-up: 2.56% (95% CI: 2.47, 2.65). In generalized linear models, overall differences in the mean proportion of patients waitlisted between intervention and control among Black patients at 12 months was 0.22% (0.02, 0.42), p<0.05. Among white patients, waitlisting declined in the control group and remained the same among intervention group facilities. Results were more pronounced among the 57% of intervention facilities considered high implementers (Figure 1, right).

**Conclusions:** The ASCENT educational and outreach intervention helped to extend the reach of this policy among U.S. dialysis facilities with low waitlisting in the population of prevalent Black patients who are most likely to benefit from the policy change.

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Evolution of Thromboelastography Parameters During Pediatric Liver Transplantation

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Background: Liver failure is characterized by abnormal bleeding and clotting as the liver produces the majority of procoagulant, fibrinolytic, and regulatory proteins of the coagulation system. Liver transplantation (LT) carries high risk of intraoperative bleeding. Thromboelastography (TEG), a global coagulation assay, measures several aspects of clot formation in real time and is used to guide blood product administration including LT. However, no data on description of TEG parameters during pediatric LT exist.

Methods: An IRB-approved retrospective review of subjects under 18 years of age undergoing LT between 2015 and 2017 was performed to describe the TEG parameters that were obtained at three time points (baseline, anhepatic and reperfusion) during LT and to evaluate blood product utilization during and immediately post-operation. Friedman Test to compare TEG parameters at the 3 timepoints, and Pearson correlation coefficients to evaluate association with blood product transfusion volumes were used.

Results: Demographic, clinical, surgical and post-surgical characteristics of 80 children that underwent LT are shown in Table 1. 39 subjects were females (49%). The majority had intrinsic liver disease 59 (74%). Two episodes of portal vein thrombosis occurred. Six subjects returned to the OR for postsurgical bleeding.

Figure 1 describe the TEG values for all 3 points during transplantation: All TEG parameters showed statistically significant change across the time-points, although those obtained during anhepatic and reperfusion times were similar: median (IQR) maximal amplitude (MA) 57.8 (50.3-64.4) vs 53.3(44.3-61.4) vs 53.8 (46.1-59.5), Alpha Angle (a) 67.9 (60.6-72.1) vs 61.4(48.5-69.5) vs 60.2 (47.9-67.8) and Citrate Kaolin (CK) R 5.2 (4.4-7.0) vs 6.2 (4.8-8.2) vs 7.1(5.6-9.0). MA and a decreased throughout the case while CK R time increased.

Summary characteristics of TEG results and correlates with intraoperative blood product transfusion volumes (Median (IQR) cc/kg body weight) are shown in Tables 2. 50 subjects (62%) received 20.8 cc/kg (10.2-34.1) fresh plasma, 36 subjects (45%) received 5.8 cc/kg (2.9 -8.7) cryoprecipitate and 29 subjects (36%) received 8.5 cc/kg (5.4-16.1) platelets. Intraoperative transfusion of any blood product correlated with nearly all baseline TEG parameters, and with anhepatic MA and alpha angle. Plasma transfusion correlated with MA at the reperfusion time.

Conclusions: This is the first descriptive analysis of TEG parameters during pediatric LT. During the surgical procedure there is transition from a hyper-coagulable state to a longer time to form the blood clot and fibrinolysis. Intraoperative TEG guidance may allow more targeted support of coagulation using better transfusion algorithms without leading to more complications. Further studies to assess the adoption of TEG during LT need to be independently evaluated along with the establishment of meaningful outcome measures.
Extracorporeal Membrane Oxygenation Use in Orthotopic Liver Transplantation as a Viable Bridge to Transplant and Tool For Intraoperative and Postoperative Rescue

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Introduction: The use of extracorporeal membrane oxygenation (ECMO) to treat cardiac and pulmonary failure in orthotopic liver transplant (OLT) patients is uncommon and poorly understood despite the high morbidity and mortality related to these complications. We present one of the largest contemporary single-center case series of adult OLT patients requiring ECMO.

Methods: This is a retrospective study of adult patients undergoing OLT at University of Chicago from January 2017 to March 2022, who required ECMO before, during, or after transplant. We excluded pediatric patients and patients undergoing simultaneous heart-liver and heart-liver-kidney transplantation. We conducted a chart review to identify relevant patient and operative factors, length of hospital stay, postoperative complications, postoperative survival days, length of time on ECMO, and mortality.

Results: A total of 273 patients underwent OLT during the study period. Eleven patients required ECMO, of which ECMO was initiated in 4 patients pre-transplant (planned), 2 patients intraoperatively (rescue), and 5 patients postoperatively (rescue). Patient and operative factors in addition to outcomes are described in Table 1. Six of the 11 patients survived to discharge following ECMO decannulation and all six are alive today. Three different types of ECMO were used: venoarterial (peripheral femoral venoarterial cannulation and central cannulation), venovenous ECMO (peripheral femoral venovenous cannulation), right ventricular assist device (RVAD) with an oxygenator (via a dual lumen cannula placed in the internal jugular so that its inflow lumen is in the SVC and outflow lumen is in the pulmonary artery).

Conclusions: ECMO may be used as a bridge to transplantation, for intraoperative rescue, and in the postoperative setting to provide mechanical support when medical management options for severe cardiopulmonary failure have been exhausted. Prior to using ECMO as a bridge to transplantation, evaluation should focus on the post-transplant reversibility of the condition requiring ECMO (e.g. advanced hepatopulmonary syndrome or severe right ventricular dysfunction). When ECMO is used for intraoperative rescue or postoperative decompensation, our outcomes are similar to previously published work. We noted improved outcomes when it is utilized for isolated hypoxemia without heart failure/vasoplegic shock. The exception to this observation was Patient 2 who had an RVAD/oxygenator placed prior to transplant for severe right ventricular dysfunction from volume overload with low pulmonary vascular resistance. In our experience, the need for rescue ECMO was unpredictable based on preoperative patient factors. Based on these results, we believe that ECMO is a viable strategy to provide additional support for patients with medically refractory but reversible hypoxemia or cardiogenic shock.

| Table 2: Correlations between TEG parameters at 3 timepoints (beginning of surgery, anhepatic phase, and reperfusion) and intraoperative blood product transfusion volumes. |
|------------------|---|---|---|
|                  | N  | FFP (oz/kg) | PLATELETS (oz/kg) | CRYO (oz/kg) |
| Beginning: MA    | 80 | -0.232*      | -0.506***         | -0.500***    |
| Beginning: Alpha Angle | 80 | -0.206      | -0.390***         | -0.433***    |
| Beginning: CXH R-min | 80 | 0.129       | 0.317**           | 0.327**      |
| Beginning: CXH R-min | 80 | 0.257*      | 0.259*            | 0.237*       |
| Anhepatic: MA    | 64 | -0.593**     | -0.425***         | -0.523***    |
| Anhepatic: Alpha Angle | 64 | -0.255*  | -0.287*           | -0.396**     |
| Anhepatic: CXH R-min | 64 | 0.289*     | 0.203             | 0.375**      |
| Anhepatic: CXH R-min | 64 | 0.039      | -0.034            | 0.103        |
| Reperfusion: MA  | 59 | -0.375*      | -0.051            | -0.113       |
| Reperfusion: Alpha Angle | 59 | -0.121    | -0.066            | -0.127       |
| Reperfusion: CXH R-min | 59 | 0.137      | 0.109             | 0.159        |
| Reperfusion: CXH R-min | 59 | 0.004       | -0.016            | -0.018       |

Abbreviations: cc (cubic centimeter), CRYO (cryoprecipitate), FFP (fresh frozen plasma), kg (kilogram), TEG (thromboelastogram)
Rates of Effective Intent-To-Donate in Nova Scotia: Mitigation of Differences by Gender and Age After Enactment of Deemed Consent Legislation

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Introduction: Some of the highest rates of deceased donation activity in the world are observed in European countries with deemed consent legislation.(1) On January 18, 2021, Nova Scotia became the first jurisdiction in North America to implement a deemed consent model with the enactment of Human Organ and Tissue Donation Act (HOTDA). This study aimed to establish rates of effective intent-to-donate before and after enactment of deemed consent legislation in Nova Scotia.

Method: Analysis of aggregate data obtained from the Nova Scotia Organ and Tissue Donation Registry. The effective intent-to-donate (%) was determined as either the proportion of eligible Nova Scotians registering an opt-in decision pre-HOTDA or the proportion of eligible Nova Scotians registering an opt-in decision or not registering an opt-out decision post-HOTDA (January 18, 2021). Donor registration data was available from April 2018 (34 months pre-HOTDA) to February 2022 (12 months post-HOTDA). This data included a demographic breakdown by gender and age ranges (19-29, 30-48, 49-64, 65+) of eligible Nova Scotians.

Results: Rates of effective intent-to-donate increased from 49.0% to 51.9% in the 34 months leading up to HOTDA enactment, and from 51.9% to 99.1% in the month of enactment (Figure 1). In the 12 months post-HOTDA, rates of opt-out increased by 0.3% to 0.5% per month resulting in an effective intent-to-donate rate of 94.4% one year following enactment. At enactment, more females than males had registered an opt-in decision (54.7% vs. 49.1%). One year following enactment, rates of effective intent-to-donate were similar in both groups (94.8% females vs. 94.6% males). At enactment, a lower proportion of people 65+ had registered an opt-in decision (40.3%) relative to other age groups (19-29 = 54.6%; 30-48 = 59.8%; 49-64 = 54.4%). One year following enactment, rates of effective intent-to-donate were similar in all age groups (19-29 = 94.7%; 30-48 = 95.7%; 49-64 = 94.6%; 65+ = 92.5%).

Conclusion: This work evaluates the impact of deemed consent legislation on effective intent-to-donate in Nova Scotia. Enactment of deemed consent legislation increased rates of effective intent-to-donate and appears to have mitigated pre-existing differences by gender and age group. Future research into the relationship between the dramatic increase in rates of effective intent-to-donate and consent rates is ongoing.

References:

Protection From the Second Warm Ischemic Injury in Kidney Transplantation Using an Ex Vivo Non-utilised Human Kidney Model and Thermally Insulating Jacket

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Introduction: Kidney transplantation is the optimal treatment for suitable patients with end-stage renal disease. The duration of surgical vascular anastomosis time, also known as second warm ischaemic time (SWIT) has now been identified as impacting both delayed graft function as well as long-term graft survival in kidney transplantation, with temperatures above 15-18°C regarded as the threshold for ischaemic injury. There is currently no commercially available method of overcoming the SWIT period through intra-operative thermal insulation. This study aims to analyse the effect of a novel biomedically engineered thermally insulating jacket, the ischaemic injury protective jacket (iiPJ) as a solution to overcoming this second warm ischaemia. The iiPJ has been previously validated with porcine kidney and this study aims to test whether the iiPJ is able to thermally insulate non-utilised human donor kidneys in an ex vivo transplant model.

Methods: An ex vivo transplantation model using a water bath regulated at 37°C to replicate average human body temperature was utilised for this study. Non-utilised kidneys were obtained and tested with and without the insulation of the iiPJ to measure the average core temperature of a kidney at 30-second intervals for 60 minutes on a temperature-time graph.

Results: The control kidney core temperature reaches the 15°C threshold temperature at 17.3±1.8 minutes and the 18°C threshold at 20.9±2.0 minutes. This time to reach the warm ischaemia threshold temperature is below the average global surgical time of 40.5±17.5 minutes. The iiPJ protected kidney reaches the 15°C threshold temperature at 44.5±1.9 minutes and remains within the 18°C threshold till 53.3±1.3 minutes. This amount to an additional thermal protection of 27.2±3.7 minutes (n=5, p=0.0017) for the iiPJ protected kidneys when compared to the current surgical practices represented by the control kidneys.

Implication and Conclusion: The iiPJ is significantly effective in reducing the thermal profile of the kidney, increasing the time available for transplantation, and minimising the time pressure on surgeons in order to reduce the occurrence of surgical complications. The iiPJ is a single-use, low-cost medical device that has the potential to become the standard of care in renal transplants. Further research regarding the biological effect of the iiPJ on the expression of biomarkers of ischaemia shall be undertaken to further strengthen the case for intraoperative thermal insulation, prior to a clinical trial, as the ideal surgical practice for kidney transplantation, surgical training, and robotic transplantation.
Investigating Galectin-3 as a Novel Therapeutic Target To Block Inflammation and Reduce Ischemia Reperfusion Injury During Vascular Composite Allograft Transplantation

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Introduction: Vascularized Composite Allograft (VCA) transplantation is a treatment option for complex injuries that leave patients with structural and functional deficits that cannot be adequately reconstructed. During transplantation, grafts are subjected to hypoxic/ischemic injury during procurement, storage, and reperfusion. Skin and muscle containing VCA are highly susceptible to ischemia reperfusion injury. Galectin-3 is an endogenous β-galactoside binding lectin known to play a role in driving inflammatory responses in response to hypoxic/ischemic stress. Blocking galectin-3 using known inhibitors including modified citrus pectin (MCP) has been shown in animal models to reduce inflammation and fibrosis. We hypothesized that galectin-3 significantly contributes to VCA IRI and that blocking galectin-3 can serve as a novel therapeutic approach to prevent or reduce IRI. We aimed to determine the role of galectin-3 in VCA ischemia reperfusion injury and the effect of blocking galectin-3 using MCP in syngeneic VCA models.

Method: Male Brown Norway rats underwent syngeneic hind limb transplantation following 0, 6 or 24 hours of cold ischemia time. A group of rats receiving hind limbs subjected to 24 hours of static cold storage were treated with MCP (1% w/v) in the drinking water starting one week prior to transplantation. Recipient serum and donor VCA tissues were collected at end-of-study 6 days post transplantation. Sera and tissues collected from naive Brown Norway rats were included as controls. Sera levels of galectin-3 were determined by sandwich ELISA (Novus Biologics, Inc). Galectin-3 expression in the muscle was determined by Western Blotting. The degree of inflammation in the muscle tissue was determined by H&E.

Results: Sera galectin-3 levels averaged 0.854±0.557ng/ml in naïve BN rats (n=7), 4.232±1.543ng/ml in recipients of grafts transplanted immediately without static cold storage (n=3), 12.86±1.292ng/ml in recipients of grafts subjected to 6 hours cold storage without MCP treatment (n=3), 20.10±3.185ng/ml in recipients of grafts subjected to 24 hours cold storage without MCP treatment (n=6), and 12.77±2.098ng/ml in recipients of grafts subjected to 24 hours cold storage with MCP treatment (n=9) (Figure 1A). Galectin-3 expression in the VCA muscle increased according to the extent of cold ischemia. MCP treatment decreased muscle galectin-3 expression (Figure 1B) and inflammation in the muscle (Figure 2) post transplantation.

Conclusion: Galectin-3 levels significantly increased in recipient sera and donor muscle within a week in rats transplanted with donor VCA grafts subjected to prolonged ischemia. Blocking galectin-3 using MCP can reduce the amount of galectin-3 in circulation and muscle tissue post transplantation and may decrease inflammation associated with VCA IRI. Galectin-3 may serve as a novel therapeutic target to reduce inflammation associated with ischemic injury and improve VCA outcomes.

DOD CDMRP RTRP W81XWH1910163 RT180168.
Using a New Preservation Solution Called Perla for Kidney Transplantation

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Background: The composition of organ preservation solutions is crucial for maintaining graft integrity and is directly related to morbidity and survival after transplantation. The aim of this study is to compare the function of rat kidney grafts after organ storage in the new organ preservation solution PERLA® (patented by Barcelona University; PCT/ES2009/000267) and the gold standard solution of University of Wisconsin (UW). On the one hand, UW contains HES (inducing erythrocyte aggregation), high-K+ concentration (causing hyperkalemic cardiac arrest) and some drugs like allopurinol, GSH or adenosine which does not confer any protection. On the other hand, PERLA® solution is a high Na+/low K+ liquid including PEG-35 (1 g/L), trimetazidine (1 µM), carvedilol (10 µM) and tacrolimus (5 µM). These last three compounds have been reported as strong modulators of ischemia-reperfusion (I/R) injury.

Methods: To assess oxidative stress after cold storage, kidney grafts have been preserved for 18h at 4°C in either UW or PERLA® solutions and then oxidative stress markers were determined in renal tissues. To evaluate kidney injuries and oxidative stress after graft reperfusion, rat kidneys were harvested, stored in cold UW or in PERLA® solutions for 18h and then transplanted heterotopically for 6h. In order to determine the potential benefits of PERLA® solution, antioxidant enzymes (superoxide dismutase–SOD; glutathione peroxidase-GPX; reduced glutathione-GSH; catalase-CAT) activities and oxidative stress parameters (malondialdehyde-MDA; conjugated dienes-CD; formation and protein sulfhydryl-PSH) were determined in renal tissue. In addition, cytolyis (measuring lactate dehydrogenase-LDH levels in plasma) and kidney function (quantifying plasma concentrations of uric acid and creatinine) were determined.

Results: Kidney transplantation using UW solution led to a significant increase in the oxidative stress and renal lesions parameters and, in parallel, to a decrease in the activities of all the antioxidant enzymes. Our results showed that preservation of kidneys in PERLA® solution significantly attenuates oxidative stress parameters after cold storage and reperfusion. Indeed, we found a significant decrease in oxidative damage indicator (MDA, CD and CP) and a significant increase in antioxidant indicators (GPx, GSH, CAT, SOD and PSH). Moreover, PERLA® solution decreases kidney injury after reperfusion (Creatinine, LDH and uric acid).

Conclusion: Our study shows that PERLA solution was more effective in preserving rat’s kidney grafts than the gold standard UW solution. PERLA preservation solution was able to reduce oxidative stress and to improve the functional recovery of kidney grafts during cold ischemia and after transplantation.
CHOP Promotes ROS-Mediated Liver Ischemia and Reperfusion Injury by Inhibiting Mitophagy in Hepatocytes

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Background: Liver ischemia and reperfusion (IR) injury represents a major risk factor in both partial hepatectomy and liver transplantation. CCAAT/enhancer-binding protein homologous protein (CHOP) is a key regulator of cell death, its precise molecular basis in regulating hepatocyte death during liver IR has not been delineated.

Methods: Hepatocellular CHOP deficient mice were generated by bone marrow chimera models using global CHOP knockout mice. Liver partial warm ischemia model and hypoxia/reoxygenation (H/R) model of primary hepatocytes were applied. Liver injury and mitophagy related signaling pathways were investigated. IR-stressed patient liver tissues and serum samples were analyzed as well.

Results: Mice with hepatocellular CHOP deficiency exhibited alleviated cell death, decreased reactive oxygen species (ROS) expression and enhanced mitophagy in hepatocytes after IR, confirmed by in vitro studies of hepatocytes after H/R. Mitochondria ROS scavenge by Mito TEMPO effectively attenuated hepatocyte death and liver IR injury of WT mice, whereas no significant effects were observed in hepatocellular CHOP-deficient mice. CHOP depletion upregulated dynamin-related protein 1 (Drp1) and Beclin-1 activation in the mitochondria of hepatocytes leading to enhanced mitophagy. Following IR, increased CHOP expression and impaired mitophagy activation were observed in the livers of patients undergoing hepatectomy. N-acetylcysteine (NAC) pretreatment significantly improved the liver function of patients after surgery.

Conclusion: IR-induced CHOP activation exacerbates ROS-mediated hepatocyte death by inhibiting Drp1-Beclin-1-dependent mitophagy. National Natural Science Foundation of China (82071798, 81901628, 81600450), National Science Foundation of Jiangsu Province (BK20191490), CAMS Innovation Fund for Medical Sciences (No.2019-I2M-5-035).

Effects of Argon Inhalation on Reducing Pulmonary Warm Ischemia-Reperfusion Injury in CLAWN Miniature Swine

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Background: Ischemia-reperfusion injury (IRI) remains a major cause of early death in lung transplantation. In addition, warm ischemia of the donor organ is inevitable when transplanting from DCD donor, and it is important to develop new strategies for reducing warm IRI. The cytoprotective effects of chemically inert noble gases such as argon (Ar) have been demonstrated. Ar is particularly safe and cost-effective because it is non-anesthetic and the third most abundant gas in the atmosphere, suggesting higher safety levels and lower cost advantages. The inhibitory effect of IRI has been reported in small animal models of various organs, but there are conflicting reports on the effect in large animal models. In this study, we evaluated the cytoprotective effect and safety of Ar inhalation using large animal model of pulmonary warm IRI model.

Methods: Ten CLAWN miniature swine were evenly divided into two groups (Ar-treated and control group). In both groups, warm ischemia was induced for 90 minutes by clamping the left bronchus, pulmonary artery and veins. Animals were inhaled with either 70% Ar (Ar-treated) or 70% nitrogen (control) in 30% oxygen for 360 minutes throughout the procedure. Lung function and structure were serially assessed via the ratio of partial pressure of oxygen to fractional inspired oxygen (pO2/FiO2) measured by both arterial blood and pulmonary vein (PV), chest X-ray (CXR) and lung biopsy, as well as the presence of side effects.

Results: Ar inhalation dramatically decreased lung injury associated with ischemia and reperfusion without apparent adverse effects. In the control group, 90 minutes of warm ischemia resulted in a significant decrease in pO2/FiO2 by arterial blood, from 568 +/-12 mmHg before ischemia to 272 +/-39 mmHg 2 hours after reperfusion (p<0.05). In sharp contrast, animals in the Ar-treated group had no significant change in pO2/FiO2 by arterial blood despite 90-min ischemia (563 +/-18 mmHg before ischemia to 431 +/-49 mmHg 2 hours after reperfusion). Moreover, pO2/FiO2 by PV showed well-maintained lung function in the Ar-treated group (331 +/-40 vs. 186 +/-17 mmHg at 2 hours, p<0.05; 519 +/-19 vs. 292 +/-33 mmHg at 2 days after reperfusion, p<0.05). In addition, histological scores of lung biopsies (calculated based on four items: cellular infiltration, intralobular edema, fibrin exudation, and hemorrhage) were significantly better in the Ar-treated group for both 2-hour and 2-day biopsies after reperfusion. The evaluation of serum and biopsy samples suggested that anti-oxidant and anti-apoptosis were the main mechanisms of Ar inhalation.

Conclusion: In this study, we demonstrated for the first time the inhibitory effect of perioperative Ar inhalation on pulmonary warm IRI in large animals. In order to apply this new therapy to clinical practice, further detailed analysis of the mechanism and evaluation using ischemic models including cold storage are required in the future.
Necroptosis Plays a Role in Acute Kidney Injury (AKI) and the Progression to Renal Fibrosis Following Ischemia Reperfusion Injury (IRI)

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Introduction: In kidney transplantation, ischemia reperfusion injury (IRI), a type of acute kidney injury (AKI), is associated with poorer outcomes including delayed graft function, rejection and chronic kidney disease (CKD) with fibrosis. Therapies to reduce AKI and CKD following transplantation have been investigated but none has been translated into clinical practice. Here we examined necroptosis, a pathway of regulated necrosis that has been implicated in kidney IRI. Necroptosis is triggered by recruitment of the intracellular kinases RIPK1 and RIPK3 and activation of the pseudokinase MLKL. Active MLKL causes cell death by plasma membrane rupture, driving “necroinflammation”. RIPK1 and RIPK3 may also have a cell death-independent role in the development of kidney fibrosis. The aims of this study were to (1) investigate the role of necroptosis in a mouse IRI model of AKI, using knock-out mice and small molecule inhibitors, and (2) determine whether inhibition of RIPK1 or RIPK3 after AKI interferes with the progression to CKD.

Methods: AKI model: 10-12 week old male MLKL KO mice and wild type (WT) littermates underwent right nephrectomy followed by 18, 20, 22 or 24 min left kidney ischemia. Samples were collected at 24 h to assess renal injury, inflammation and necroptosis. In a separate experiment using the 18 min model, WT mice were treated either before or after IR with a RIPK1 inhibitor Nec-1s, a RIPK3 inhibitor GSK872, or vehicle. CKD-after-AKI model: This model was adapted from the AKI 18 min model by (i) omitting right nephrectomy, (ii) delaying the endpoint to 28 days, and (iii) extending the analyses to include renal fibrosis (Masson’s trichrome staining) and relevant gene expression. WT mice were treated with Nec-1s, GSK872 or vehicle daily on days 3-9.

Results: In the AKI model, expression of necroptotic (RIPK1, RIPK3 and MLKL), kidney injury (KIM-1, NGAL) and inflammatory (IL-6, IL-1β, IL-33, TNFα) genes was significantly upregulated following moderate (18 min) and severe (20-24 min) ischemia. MLKL KO mice were protected from moderate but not severe IRI, with lower creatinine (µmol/L) (47.13±6.28 vs 80.78±10.45, p=0.007) and less tubular injury (%) (16.79±2.80 vs 26.95±3.68, p=0.048) compared to WT littermates. WT mice receiving Nec-1s before or after IR showed reduced creatinine and tubular injury compared to vehicle controls, whereas GSK872 was not protective.

In the CKD-after-AKI model, vehicle-treated WT mice showed significant renal fibrosis at 28 days compared to sham (fibrosis score 28.68±1.25 vs 2.33±0.11, p=0.0025), with increased expression of RIPK1 (p=0.0079), RIPK3 (p=0.0025), and the pro-fibrotic genes TGFβ (p=0.0025), HIF1α (p=0.0025) and Col-I (p=0.0025). Inhibiting RIPK1 or RIPK3 on days 3-9 resulted in reduced fibrosis.

Conclusion: Our data support a role for necroptosis in AKI and fibrosis following IR, and identify inhibition of the necroptosis pathway as a potential therapeutic strategy.

NHMRC scholarship GNT1168307.
Background: Static cold preservation remains the cornerstone for optimizing donor livers during procurement. The choice of preservation solutions, University of Wisconsin (UW) versus histidine-tryptophan-ketoglutarate (HTK) solutions, remains controversial. Recent ILTS guidelines have recommended to avoid utilizing HTK solutions during donation after circulatory death (DCD) liver procurement based on older data. Given concerns in the existing literature of confounding due to the learning curve for HTK use and of period effects including increasing marginal donor liver use and changes in listing indications for liver transplantation (LT), we aimed to ascertain the updated short- and long-term graft outcomes between HTK and UW solutions among LT recipients.

Methods: First-time adult (≥18 years) deceased-donor LT recipients between January 1, 2006 and December 31, 2020 were identified from the US national transplant registry (UNOS) database. The LT recipients were divided into 2 primary groups, UW and HTK, and analyzed in 3 eras: 2006-2010; 2011-2015; and 2016-2020. DCD LT and donation after brain death (DBD) LT recipients were analyzed separately. Kaplan-Meier survival analysis and Cox proportional hazards modeling were utilized to compare UW vs. HTK outcomes.

Results: Among the 5,956 DCD LTs, 3,873 (65.0%) and 1,944 (32.7%) used UW and HTK, respectively. The practice of DCD LT also increased 3-fold over the study time period with the annual number increasing from 269 in 2006 to 828 in 2020. The practice of DBD LT remained 3-fold over the study time period with the annual number increasing from 269 in 2006 to 828 in 2020. The practice of DBD LT also increased with the annual number increasing from 5,044 in 2006 to 6,711 in 2020. There was no difference in 1- or 5-year graft survival rates between UW and HTK groups among DCD LTs in the 2006-2010; 2011-2015; and 2016-2020 eras. DCD LT and donation after brain death (DBD) LT recipients were analyzed separately. Kaplan-Meier survival analysis and Cox proportional hazards modeling were utilized to compare UW vs. HTK outcomes.

Conclusions: The latest US transplant data suggests that HTK is now superior to UW for preserving DCD livers. These data support the use of HTK in DCD LT and contradict the latest ILTS guidance. Future prospective controlled trials in DCD LT are required to confirm this finding.
422.10

PROTEINASE3 (PR3) Promotes Hepatic Ischemia Reperfusion Injury Through Regulating Hepatocytes Pyroptosis

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Background: Increasing evidence showed that hepatic ischemia-reperfusion injury (IRI) is a typical inflammatory response involving a complex web of interactions between various cellular and molecular signals. We here intended to investigate the effect of the neutrophil serine proteases proteinase-3 (PR3) in hepatic IRI and to explore the underlying mechanisms.

Methods: The association of PR3 expression with hepatic inflammatory response were investigated both in human liver transplantation and mouse hepatic IRI model. The direct role of PR3 in regulating hepatic IRI was studied in PR3 knockout mice IRI model in vivo and primary cells in vitro.

Results: Our results showed that the expression of PR3 was increased in human and mouse liver after hepatic IRI and mainly detected in neutrophils. Over expression of PR3 was associated with severe histological damage, hepatic apoptosis, higher expressions of inflammatory cytokines/chemokines, more infiltrations of macrophages and neutrophils. In vivo functional study, the knockout of PR3 reduced hepatic histological damage, apoptosis, ALT level and inflammatory response after liver IRI. In the neutrophil depletion mice IRI model, the neutrophil from PR3 KO mice adopt transferred reduced hepatic injury and inflammatory response after IRI compared to neutrophil from PR3 WT mice. Furthermore, the knockout of PR3 attenuated cell pyroptosis after hepatic IRI, and the decreased cell pyroptosis was found in hepatocytes, evidenced by decreased expressions of Cleaved Caspase3 and GSDME. In vitro functional study also confirmed that PR3 can promote hepatocytes pyroptosis and injury. Moreover, the PR3 contributed to the hepatocytes pyroptosis dependent on the Caspase3 Cleavage.

Conclusions: The neutrophil PR3 may induce hepatic IRI through promoting hepatocytes pyroptosis via Caspase3 Cleavage. PR3 may be the potential therapeutic target of attenuating hepatic IRI.

422.11

Instant Post-reperfusion Thromboinflammation in Clinical Kidney Transplantation and Its Possible Impact on Outcome

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Introduction: During the process of transplantation, detrimental events such as ischemia inflict harm to, and change the cell phenotype of organs, which increases the susceptibility to an early innate immune attack post-reperfusion. Here, we present data on a detailed systematic characterization of this early response post-reperfusion and its possible impact on outcome after kidney transplantation.

Method: Sixty-three consecutive kidney transplant recipients were included. Twenty-six (41%) and 37 (59%) patients received kidneys from living (LD) and deceased donors (DD), respectively. Fifteen DD-kidneys (41%) were preserved with hypothermic machine perfusion (DDmp) and 22 (59%) were preserved in cold storage (DDcs). Four venous EDTA blood samples were collected intra-operatively at baseline (pre-reperfusion from the external iliac vein) and at 1-, 10- and 30-minutes post-reperfusion from the proximal portion of the transplant vein. Samples were handled according to a meticulous and standardized routine including immediate and sustained cooling with subsequent storage of plasma samples at -80 °C. Biomarkers for the complement, coagulation and contact cascade systems were measured. Clinical outcome data for a total of 24 months were collected. Non-parametric analysis of variances on aligned rank transformed data and receiver operating characteristics (ROC) analyses were used.

Results: Patient and graft survival did not differ between DD and LD by 24 months. There were no differences in donor age/BMI between LD and DD recipients. The median kidney-donor-risk-index did not differ between DDcs and DDmp (1.56 vs 1.5). Median cold ischemic times in DDcs and DDmp were 11.4 and 13 hours, respectively. Overall, 6 patients (9.5%, all DD-recipients) experienced delayed graft function (DGF). Thromboinflammation, defined as co-activation of complement (sC5b-9), coagulation (FXIIa, thrombin) and contact (FXIIa, KX) cascade systems, was detected instantly post-reperfusion in DD-kidneys (predominantly in DDcs), while being largely absent in LD-kidneys. Analyzing the slopes for serum-creatinine and eGFR between 3 to 24 months post-transplant, the release of sC5b-9 at 30 min post-reperfusion correlated with a higher serum-creatinine and lower GFR slope in DDcs, but not in LD and DDmp. Thrombin, sC5b-9, FXIIa and FXIIIa were predictive for DGF, de novo DSA and rejection.

Conclusion: Instant post-reperfusion thromboinflammation (IPRT) occurs in DD-kidneys exposed to ischemia, while being largely absent in LD-kidneys. This early innate immune response may be associated with impaired midterm graft function, even in the current population with a low burden of ischemia. Furthermore, markers of IPRT were predictive for outcome measures such as DGF and rejection. Lastly, hypothermic machine perfusion seems to reduce IPRT.
Adoptive Tolerogenic Dendritic Cell Therapy Protects Against Renal Ischemia Reperfusion Injury

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Aim: Elucidate the pathways through which tolerogenic dendritic cell (TolDC) therapy provide protection against renal ischemia reperfusion injury (IRI).

Method: Ex-vivo TolDC (+/- lipopolysaccharide (LPS) stimulation) were derived from C57BL/6 bone marrow and cells were assessed for flow, functional (mixed lymphocyte reaction and TolDC-renal tubular epithelial cell (RTEC) co-cultures), and transcriptomic phenotype. Male, C57BL/6 mice underwent bilateral renal IRI (20 minutes/36°c) and treated perioperatively with adoptive cell therapy (live/CD11c-enriched TolDC or LPS-TolDC cells) or PBS control. Mice were also subjected to bilateral IRI (22 minutes/36.5°c) to assess the impact of liposomal clodronate on cell therapy efficacy. Analysis of renal function, histology, biomolecular phenotyping, and spatial transcription was performed 24-hours post-operatively.

Results: Gene set enrichment analysis (GSEA) revealed upregulated immune pathways in LPS-TolDC vs TolDC, supporting a semi-activated state. Elevated PDL1:CD86 MFI ratio (p<0.05), increased supernatant IL-10 with reduced IL-12p70 (p<0.001) and lymphocyte hypoproliferation was seen with both TolDC and LPS-TolDC compared to controls. Co-cultured RTECs had lower TNF-alpha/KIM-1/LCN2 mRNA expression (p<0.01) in response to LPS. Compared to controls, mice treated with LPS-TolDC, but not TolDC, were protected against AKI, with lower serum creatinine (p=0.006 vs p=0.28 respectively), histological injury and cell death scores (p<0.05) (Figure 1). Depletion of recipient myeloid cells with liposomal clodronate did not impair the reno-protective capacity of cell therapy (creatinine 30.6±19mmol vs 155±44.7mmol/L, p<0.001). LPS-TolDCs were more likely to localise to the kidney compared to TolDCs (7.7 vs 3.5 % CD45+, p<0.00) by flow cytometry tracking. Kidney mRNA revealed reduced pro-inflammatory and antioxidant expression (IL-6/TNF-alpha/CCL2/SOD/inducible-NOS, p<0.05), which was supported and further defined by distinct clusters shown via spatial transcription. GSEA revealed reduced innate, adaptive and cell death pathways, with upregulation of antioxidant pathways in kidneys from mice who received LPS-TolDC therapy (Figure 2).

Conclusion: LPS-TolDCs demonstrate potent protection against renal IRI and is associated with reduced kidney inflammation, oxidative stress, and cell death. This evidence supports further investigation into cell therapy to modulate IRI severity.

Figure 1: A) overview of adoptive cell therapy in renal IRI. B) Serum creatinine, C) H&E injury scores and D) TUNEL staining results between groups shown. Representative H&E images in E) from PBS and TolDC (top left and right); LPS-TolDC and AlloTolDC (bottom left and right) and F) TUNEL stains control (top) and LPS-TolDC (bottom) kidneys.
Characteristics and Long-term Outcomes of Female Kidney Donors

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Introduction: Almost twice as many females donated a kidney in the United States between 1988-2021. Yet, detailed information regarding their long-term outcomes are sparse. Importantly, there has been no studies that addressed the possible contribution of pregnancy or gestational complications. Therefore, we compared mortality, cardiovascular disease (CVD), and development of hypertension, diabetes, proteinuria, reduced estimated glomerular filtration rate (eGFR) and kidney failure in 4,995 females and 3,881 male donors.

Methods: We studied female donors in a retrospective cohort study of kidney donors who donated between 1963 to 2007 at three US transplant centers as a part of The Renal and Lung Living Donor Evaluation Study. Mortality, CVD, diabetes, hypertension, proteinuria and reduced eGFR for the entire cohort and for females after adjusting for pregnancy and gestational complications were studied using multivariable analysis.

Results: At 17.4±10.8 years after donation, 4.1% of female donors and 5.8% of male donors were deceased, aHR 0.53 (95% CI 0.37, 0.76), p = 0.001; 6.5% vs. 8.0% developed diabetes, aHR 0.98 (95% CI 0.71, 1.32), p = 0.88; and 32.5% vs. 42.5% developed hypertension, aHR 0.87 (95% CI 0.77, 0.97), p = 0.02. The multivariable risks of death, CVD and hypertension were higher in male donors. The risk of reduced eGFR, proteinuria and ESKD were, however, comparable in both sexes. A similar proportion of female and male donors developed eGFR < 30 mL/min/1.73m² or kidney failure; 1.6% vs. 1.9%, aHR 0.68 (95% CI 0.34, 1.35), p = 0.98 (Figure 1, Figure 2). Donors with pregnancies prior to donation and gestational complications (compared to nulliparous donors) were at increased risk for this composite outcome; aHR 4.02 (95% CI 1.24, 13.02), p=0.02 and aHR 6.06 (95% CI 1.59, 23.15), p= 0.01, respectively.

Conclusions: These results demonstrate that the overall risk of kidney failure is similar in female and male kidney donors. Pre-donation pregnancies and gestational complications were associated with a 4- to 6-fold increased risk of eGFR <30mL/min/1.73m² or ESKD compared to those without prior pregnancies. Our results are at odds with those previous studies that stated that males are at an increased risk of CVD and faster progression to ESKD. We believe the difference may stem from accounting not only for post-donation events such as diabetes and hypertension but also for prior pregnancies and gestational complications.

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Figure 2: A) Spatial transcriptomic and UMAP projections from 6 mice kidneys (n=2 from PBS/ToI1DC/LPS-ToI1Dc) and B) enriched pathways for each cluster in a cumulative bar graph.
423.2

**Patient and Graft Survival After A1/A2-Incompatible Living Donor Kidney Transplantation**

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Kayleigh Herrick-Reynolds1, Laura B. Zeiser1, Sile Yu1,
Niraj M. Desai1, Fawaz Al Ammary2, Kyle Jackson1,
Dorry L. Segev1,3,4, Allan B. Massie1,3.
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**Background:** ABO type B and O kidney transplant candidates often have increased difficulty identifying a compatible donor for living donor kidney transplantation (LDKT) and are harder to match in kidney paired donation (KPD) registries. A2-incompatible (A2i) LDKT increases access to LDKT for these patients. Kidney transplantation across the A2 barrier (A2 -> O, A2 -> B, A2B -> B) is believed to be safer than that across the A1 barrier (A1 -> O, A1 -> B, A1B -> B) because A2 kidneys express fewer A antigens on their renal endothelial surfaces. However, the differential risk of A2i LDKT and its relative benefit when compared to A1-incompatible (A1i) LDKT, if any, remains unknown. To better inform living donor selection, we evaluated the association between A2i LDKT and patient and graft survival.

**Methods:** We used inverse probability weighted Cox regression to compare mortality, death-censored graft failure, and all-cause graft loss in A2i vs. ABO-compatible (ABOc) recipients. These methods were repeated to compare mortality, death-censored graft failure, and all-cause graft loss between A1-incompatible (A1i) vs. comparable ABOc LDKT recipients.

**Results:** Using data from the Scientific Registry of Transplant Recipients (SRTR) 2000-2019, we identified 345 A2i LDKT recipients. Mortality was comparable among A2i and ABOc recipients; weighted 1/5/10-year mortality was 1.0%/7.7%/24.3%, respectively, among A2i LDKT recipients vs. 1.8%/8.7%/23.1%, respectively, among comparable recipients in the ABOc LDKT weighted cohort (wHR 0.75, 1.02, 1.40; p=0.9). However, A2i recipients faced higher risk of death-censored graft failure; weighted 1/5/10-year graft failure was 7.9%/16.4%/28.3% for A2i vs. 2.2%/9.7%/20.4% for ABOc recipients (wHR in year 1 = 2.05, 3.76, 6.88; through year 5 = 1.23, 1.98, 3.19; through year 10 = 1.13, 1.67, 2.46). By comparison, 1/5/10-year weighted hazard ratios for death-censored graft failure among A1-incompatible recipients were 0.16, 4.70, 19.07/0.47, 1.59, 5.35/0.42, 1.21, 3.53.

**Conclusions:** This registry analysis considered the differential risk of A2i LDKT in the United States and demonstrated comparable mortality to ABOc LDKT recipients, but an increased risk of death-censored graft failure for A2i LDKT recipients, particularly in the first year post-transplant. Nonetheless, A2i LDKT remains an excellent treatment option, providing access to LDKT for patients who must otherwise remain on the waitlist in hopes of receiving DDKT. Our findings further the field’s understanding of the risks and benefits of A2i LDKT, and should inform patient counseling, KPD matching algorithms, and post-operative monitoring procedures in the future.

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Long-term Outcomes Following HLA-Incompatible Living Donor Kidney Transplantation

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Introduction: Incompatible living donor kidney transplantation (ILDKT) offers a survival benefit compared to dialysis for patients with donor specific antibody (DSA) who do not have a compatible living donor. Longer-term outcomes have not been characterized in this population, but must be quantified to inform treatment selection for patients with an incompatible willing donor, and counseling for ILDKT recipients.

Method: We compared 1,406 ILDKT to 17,542 compatible LDKT (CLDKT) recipients using a 25-center cohort from the United States 1997-2016, linked to national registry data (SRTR). Participating centers classified ILDKT recipients as positive Luminex, negative flow crossmatch (PLNF, n=376); positive flow, negative cytotoxic crossmatch (PFNC, n=687); or positive cytotoxic crossmatch (PCC, n=343). We used multivariable Cox regression to quantify the risk of mortality and death-censored graft failure (DCGF), and multilevel mixed-effects linear regression to evaluate eGFR decline (CKD-EPI creatinine equation 2021) in ILDKT and CLDKT recipients.

Results: The cumulative mortality risk for CLDKT, PLNF, PFNC, and PCC was: 1.6%, 1.9%, 3.2%, and 8.2% at one year; 22.5%, 18.4%, 29.4%, and 36.1% at ten years; and 39.1%, 36.1%, 45.4% and 51.6% at fifteen-years (p<0.001) (Figure 1A). Although this translated to an equivalent mortality risk for PLNF recipients (aHR=0.830.961.12, p=0.6) after adjustment, PFNC and PCC recipients had a 1.48-fold (aHR=1.301.481.68, p<0.001) and 1.66-fold (aHR=1.331.662.08, p<0.001) higher risk compared their CLDKT counterparts, respectively. The cumulative risk of DCGF for CLDKT, PLNF, PFNC, and PCC was: 1.9%, 2.1%, 3.4%, and 11.1% at one year; 16.8%, 20.5%, 33.1%, and 41.0% at ten years; and 25.5%, 33.1%, 45.2% and 52.5% at fifteen-years (p<0.001) (Figure 1B). After adjustment, this translated to higher DCGF across all levels of DSA strength (aHR PLNF=1.141.411.73, PFNC=1.491.711.95, PCC=1.612.082.67; p for all≤0.001). Conversely, ILDKT and CLDKT recipients had comparable average eGFR immediately post-transplant (difference=-4.22-1.511.20 mL/min/1.73m2, p=0.3). However, ILDKT recipients had faster decline in eGFR per year compared to CLDKT recipients (difference in slope=-1.06-0.76-0.47 mL/min/1.73m2 per year, p<0.001; decline over 5 years for ILDKT=-9.01-7.55-6.10 mL/min/1.73m2 vs. CLDKT=-4.19-3.74-3.29 mL/min/1.73m2).

Conclusion: Patient and graft survival following ILDKT is good through fifteen years post-transplant, supporting this modality, but survival is worse compared to CLDKT recipients. ILDKT recipients bear close monitoring to maximize graft life.

This work was supported by grant numbers K01DK101677 (Massie) and R01DK98431 (Segev) from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Dr. Segev is supported by the K24AI144954 (Segev) from the National Institute of Allergy and Infectious Diseases (NIAID).

Table 1. Failure estimates and weighted hazard ratios (wHRs) for mortality and graft failure in the comparison between A2-incompatible (A2I) and ABO-compatible (ABO) living donor kidney transplant recipient outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>A2I</th>
<th>ABO</th>
<th>wHR</th>
<th>p-value</th>
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<tr>
<td>Mortality</td>
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<td></td>
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<td></td>
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<tr>
<td>1 year</td>
<td>1.0%</td>
<td>1.8%</td>
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<td>5 year</td>
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<td>10 year</td>
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<td>0.9</td>
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<tr>
<td>15 year</td>
<td>37.4%</td>
<td>38.7%</td>
<td>0.97</td>
<td>0.7</td>
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<tr>
<td>Overall</td>
<td>--</td>
<td>--</td>
<td>0.89</td>
<td>0.7</td>
</tr>
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</table>

| Death-Censored Graft Failure | | | | |
| 1 year | 7.9% | 2.2% | 0.76 | <0.001 |
| 5 year | 16.4% | 9.7% | 1.18 | <0.01 |
| 10 year | 28.3% | 20.4% | 1.17 | <0.01 |
| 15 year | 38.8% | 30.1% | 1.14 | 0.02 |
| Overall | -- | -- | 0.92 | 0.03 |

| All-Cause Graft Loss | | | | |
| 1 year | 8.2% | 3.7% | 1.26 | <0.01 |
| 5 year | 21.9% | 16.1% | 1.15 | 0.03 |
| 10 year | 40.6% | 35.8% | 1.13 | 0.01 |
| 15 year | 56.3% | 53.7% | 1.15 | 0.02 |
| Overall | -- | -- | 0.87 | 0.3 |

Table 2. Failure estimates and weighted hazard ratios (wHRs) for mortality and graft failure in the comparison between A2-incompatible (A2I) and ABO-compatible (ABO) living donor kidney transplant recipient outcomes.

<table>
<thead>
<tr>
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<th>wHR</th>
<th>p-value</th>
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<td>15 year</td>
<td>50.5%</td>
<td>38.7%</td>
<td>0</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td>Overall</td>
<td>--</td>
<td>--</td>
<td>0</td>
<td>0.8</td>
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</table>

| Death-Censored Graft Failure | | | | |
| 1 year | 9.7% | 2.2% | 1.14 | 0.03 |
| 5 year | 12.7% | 9.7% | 1.07 | 0.5 |
| 10 year | 18.9% | 20.4% | 1.06 | 0.7 |
| 15 year | 18.9% | 30.1% | 1.06 | <0.9 |
| Overall | -- | -- | 1.06 | <0.9 |

| All-Cause Graft Loss | | | | |
| 1 year | 9.7% | 3.7% | 1.26 | <0.01 |
| 5 year | 13.3% | 16.1% | 1.06 | <0.9 |
| 10 year | 24.5% | 35.8% | 1.15 | 0.6 |
| 15 year | 62.7% | 53.7% | 1.08 | 0.9 |
| Overall | -- | -- | 1.08 | <0.9 |
Raising the Potential of Transplantation With a KPD Collaborative Program

Juliana Bastos1, David JB Machado PHD2, Gustavo F Ferreira PHD1, Thais Freesz1, Helcio Rodrigues2, Renata P Souza2, Raquel Moreira1, Alexandre A Pires1, Vinicius S Colares PHD1, Camila M Assunção1, Elias David-Neto PHD2.

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Purpose: Up to 30% of potential living donor/recipient pairs cannot proceed to live donor kidney transplantation (LDKT) for immunological reasons (ABO incompatibility or positive crossmatch). Kidney Paired Donation (KPD) programs have been conducted in various countries for over 20 years as an alternative for these patients. Our goal was to estimate the potential of paired transplantation when increasing the pool of pairs by collaboration between 2 centers in Brazil.

Methods: We conducted simulated match-runs involving 2 centers: Santa Casa de Misericórdia de Juiz de Fora (SC) and Hospital das Clínicas da Universidade de São Paulo (HC). At SC, all the contraindicated donor-recipient pairs because of a positive crossmatch between January 2013 - February 2022 and whose recipients are still on the waitlist were included (N= 28 recipients and 39 donors). At HC, the pool is composed of pairs enrolled in a KPD study protocol that already performed its first paired transplant in March 2020 (N= 25 recipients and 28 donors). We used the StanfordKPD platform to optimize transplant numbers favoring high PRA recipients matches. Four acceptable ranges of DSAs MFI were established (<500, <1500, <3000 and <5000), three types of programs (accepting only 2-way exchanges; 2-and-3-way exchanges and N-way exchanges) and we also evaluated the possibility of collaboration between centers.

Results: The demographic data of both pools are shown in Table 1. The results of various KPD match-runs are shown in Table 2. As was expected, the number of transplants increases when allowing longer chains, higher MFI thresholds and collaboration between the centers. Despite the high median PRA in the pool, the StanfordKPD platform was able to find a match for up to 64% of the recipients when allowing MFI <5000. This is especially possible when we combine KPD with desensitization.

Conclusions: A KPD program can enable kidney transplant for hard-to-match patients, that tend to accumulate on the waitlist. The probability of finding a match rises with the increase of the pool of pairs and the flexibilization of the acceptance criteria.
KPD in STALYC Countries

David JB Machado PhD², Juliana Bastos¹, Alexandre Pires¹, Camila M Assunção¹, Vinicius S Colares PhD¹, Gustavo F Ferreira PhD¹, Elias David-Neto PhD².
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Introduction: Kidney paired donation (KPD) represents a strategy for increasing the number of living donor kidney transplants (LDKT), offering an incompatible donor/recipient pair the chance to exchange with another pair in the same situation. In Europe, this kind of transplant currently represents 8% of total LDKT, and in the USA account for 16.2%. This study aimed to evaluate the situation of KPD in the countries affiliated with STALYC.

Methods: We searched for “kidney paired donation”, “kidney exchange” and each Stalyc countries’ names in PubMed. Due to the paucity of results, we extended our search to Scielo and also added the spanish terms: “donacion renal cruzada”, “donacion renal pareada”, “trasplante cruzado” and “trasplante pareado”. We also conducted the exact search on Google.

Results: We found data from 16 out of 25 countries searched, of which 43.7% have laws allowing KPD and 37.5% have a record of KPD activity. Unfortunately, this activity is limited to isolated cases rather than an active program in the vast majority. Data are shown in Table 1.

Conclusion: Kidney transplantation, especially from living donors, is the best and less expensive treatment for end-stage kidney disease. Active KPD programs are scarce in the Stalyc countries. Despite housing 8% of the world’s population and being composed mainly of low-to-middle income countries, in Latin America and the Caribbean patients still do not benefit from KPD and, consequently, from its full potential for LDKT.

<table>
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<tr>
<th>Country</th>
<th>Population (millions)</th>
<th>LDKT 2019 (PMP)</th>
<th>Non-related LDKT 2019 (PMP)</th>
<th>KPD activity registered</th>
<th>Legislation</th>
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<td>Argentina</td>
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<td>México</td>
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<td>República Dominicana</td>
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<td>1.6</td>
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* Bill legitimizing KPD awaiting vote
LDKT - Living donor kidney transplant
KPD - Kidney Paired Donation
APD - Alliance for Paired Donation
Salt Sensitivity in Living Kidney Donors: A New Cardiovascular Risk Factor?

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Introduction: Kidney transplantation with living donor (LKD) is associated with longer graft and patient survival compared with deceased donor organs. Until recently, it was believed that the long-term risk of end-stage renal disease (ESRD), cardiovascular events (CVE) or death in LKD is similar to or even smaller than the general population. Nonsalt-sensible (Ss) subjects over 25 years old have a mortality similar to that of hypertensive subjects, while salt-resistant (Sr) nonsensitive subjects have a longer survival.

Objective: To compare, in healthy subjects that we have studied to be a LKD, the levels of 24 hour mean ambulatory blood pressure monitoring (24 hs mABPM), kidney function and left ventricular mass index (LVMI) between Ss and Sr, before and a year after donation.

Methods: Data from 42 LKD were included. There were 34 (82%) women, with a mean age of 49 (11) years (range 26 to 66 years). None had a history of kidney disease, diabetes, CVE or hypertension. The subjects were placed on a high-salt diet containing 250 mmol Na for 7 days and on a low-salt diet containing 30 mmol Na during the following 7 days. Compliance with the diet was assessed twice a week by measurement of 24-hour urinary Na excretion (NaU). On the last day of both the high and low-salt periods, 24-hour ABPM was performed with an automated, noninvasive device. Salt-sensitivity (SS) was defined by a significant decrease (P<0.05) of 24 hs mABPM from high to low salt intake. Trans-thoracic m-mode echocardiograms were performed on the last day of the first period. LV mass was calculated according to the Penn convention and corrected for body surface area to produce the LVMI. Data with normal and nonparametric distribution were expressed as mean and standard deviation (SD) or median and interquartile range (ICR), Student t test and Wilcoxon test were used respectively, P values < 0.05 were considered to be statistically significant.

Results: SS was found in 13 of the 42 living kidney donors (31%). The Ss group were older than Sr Ss 53 (10) vs 47 (10) years, but it was not statistically significant (p=0.08). Pre-donation, with high-salt diet the 24 hs mABPM was significantly greater in Ss than in Sr, without any differences in creatinine clearance (CrCl), 24 hs NaU and 24 hs potassium urinary (KUE) excretion. On the other hand with low-salt diet we did not find any significant differences in 24 hs mABPM, CrCl, NaU and KUE between groups. LVMI was significantly greater in Ss than in Sr donors. One year after donation we found the same statistically differences in 24 hs mABPM with high-salt diet and no differences with the low-salt diet. Again LVMI was significantly greater in Ss than in Sr donors. The increase of LVMI after donation was significant only in Sr donors. One year after donation we found significantly greater LKD showed a greater LVMI than Sr ones and a greater increase one year after donation. The study of SS could be included to make kidney transplantation with living donor organs safer.

Impact of Single Centre 440 Kidney Exchange Transplantation Over 20 Years To Increase Living Donor Pool in India: A Cohort Study

Hari Shankar Meshram1, Vivek Kute1, Vineet Mishra5, Himanshu Patel1, Subho Banerjee1, Geeta Parikh6, S. Jamal Rizvi4, Ansy Patel7, Michael Rees2, Alvin Roth3.

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Introduction: In a living donor kidney transplantation (LKT) dominated transplant program, kidney exchange may be a cost-effective and valid alternative strategy to increase LKT in countries with limited resources where deceased donation kidney transplantation (DDKT) is in the initial stages. There is a data scarcity of challenges and solutions for kidney exchange in the developing world. Here, we report our experience of 440 single-center kidney exchange transplantation to increase LKT in India.

Methods: The study has been reviewed by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the Declaration of Helsinki as well as the Declaration of Istanbul. All donor-recipient pairs (DRP) gave their informed consent prior to their inclusion in the study. All pairs exchange kidneys of similar quality.

Results: Between January 2000 and February 2020, 6050 LDKT and 925 DDKT were performed at our single-center, 440 using kidney exchanges (8.5%) (350 male, 90 female recipients, and 345 female and 95 male donors). The reasons for joining kidney exchange among transplanted patients were ABO incompatibility (n = 313), sensitization (n = 88), and better HLA matching (n = 39). All donors were near relatives (wife [n = 236], husband [n = 58], mother [n = 90], father [n = 25], sister [n = 11], brother [n = 8], grandparents [n = 2], son [n = 1] and others [n = 6]). There were 164 two-way (n = 328), 23 three-way (n = 69), 4 four-way (n = 16), 1 five-way (n = 5), 2 six-way and one ten-way kidney exchange (n = 12). The state of residence of DRP was our state (Gujarat=246), and other states (n=144). There was an overwhelming preponderance of female donors (wife and mother) but similar to our LKT program. The graft survival, patient survival, biopsy-proven rejection rate, and graft function was similar to other LKT outcomes. It is important to recognize that over the 20 years our kidney exchange program has evolved into a large, advanced program with innovative approaches to further increase LKT. We credit the success of our kidney exchange program to maintaining a registry of incompatible pairs, counseling on kidney exchange, a high-volume LKT program, and teamwork.

Conclusions: Kidney exchange is legal, cost-effective, and rapidly growing for facilitating LKT with incompatible donors. This study provides large-scale evidence for the expansion of single-center LKT via kidney exchange when national programs do not exist.

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Abstracts
Live Donated Kidneys Don’t Behave Like the One Left Behind

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Introduction: Following live kidney donation (LD), the donor glomerular filtration rate (GFR) increases for the initial 5 years1, especially in younger donors. We queried whether the recipients of younger LD kidneys would have a similar eGFR increase.

Methods: The medical records of primary LD and DD adult kidney alone recipients at a single center performed between 1/1/10-6/30/21 were analyzed. 62,371 eGFR calculations (CKD-EPI) were available between 3-36 months post-transplant for 1186 recipients. Restricted cubic splines were used to analyze the trajectory of eGFR from 3-36 months post-transplant recipients of kidneys from donors 18-35, 35-55 and >55 years. Slopes were constructed separately from 3-9, 9-21 and 21-36 months. A mixed effects model was utilized to calculate predicted eGFR for donor type/age group, separately for male and female donors (21 additional recipients excluded due to lack of donor gender data). An analysis adjusting for BSA was completed with similar results. Model results are presented in Table 1. All analyses were performed in R, ver. 4.1.1.

Results: The eGFR varied by donor age and gender. Kidneys (DD and LD) from women on aggregate provided lesser eGFR than male donors (Table 1). However, predicted eGFR change was similar when grouped by gender and age of DD and LD kidneys. Compared to recipients of LD aged 35-55, DD kidneys 18-35 years had an eGFR +10.339 mL/min/1.73m² from female donors and +8.423 mL/min/1.73m² difference from males. For DD 35-55 years, -2.333 mL/min/1.73m² difference from females and -2.092 mL/min/1.73m² from males. In a separate analysis, no observed differences in the rate of eGFR change was noted from recipient age, gender or race. The p-values (Table 1) are based on an eGFR difference from 0 mL/min/1.73m², many p-values while statistically significant, may not be clinically significant. Gender is significant. Males tend to have more kidney mass and greater BSA. If the recipient is a female and the donor a male, a higher eGFR is expected, conversely in a male receiving a female kidney, 59.7% of the recipients of female kidneys were male. Of the recipients of male kidneys, 56.4% were male. Overall, a slightly higher eGFR in recipients of male kidneys at 3 months and 3 years was observed.

Conclusion: The post-donation increase of eGFR observed after live kidney donation did not occur in the recipients of LD kidneys. The overall trajectory of LD and DD kidney transplant eGFR during the first 3 post-transplant years is similar within the age/donor type groups. Donor age and gender (more likely amount of renal mass) are important factors determining eGFR.

The First 52 Global Kidney Exchange Transplants: Overcoming Multiple Barriers to Transplantation

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Introduction: Many barriers currently stand in the way of achieving international kidney exchange including: financial, regulatory, logistical, cultural, immunological and legal barriers.

Methods: The Alliance for Paired Kidney Donation serves patients in 15 countries. Ten of these countries have participated in Global Kidney Exchange (GKE) transplants in which either living donors, their kidneys or recipients have traveled internationally to achieve successful living donor kidney transplantation (LDKT). In all cases, barriers were present that prevented LDKT in the donor or recipient country of origin.

Results: Between January of 2015 and February of 2022, GKE has produced 11 chains and 4 cycles that has provided LDKT for 17 international patients from 10 countries to be transplanted, as well as 56 LDKT for patients in the United States (US). GKE chains lengths have ranged from 1 to 11; cycles have length 2 or 3. Eight GKE transplants overcame immunologic barriers, 4 financial barriers, and 5 both immunologic and financial barriers. GKE has involved 19 US transplant centers across 18 states and 38% of recipients were minorities. For US recipients 11% had blood type (BT)-A, 57% BT-O, 17% BT-B, and 14% BT-AB; for international recipients 41% had BT-A, 41% BT-O, 14% BT-B, and 4% BT-AB. For US recipients 11% had blood type (BT)-A, 57% BT-O, 17% BT-B, and 14% BT-AB; for international recipients 41% had BT-A, 41% BT-O, 14% BT-B, and 4% BT-AB. There was no significant difference between rates of readmission within 30 days after surgery were likewise collected. Descriptive statistics were performed; continuous variables were compared with ANOVA; categorical variables were compared with Chi-squared.

Conclusions: This study provides evidence that postoperative renal function and readmission rates does not vary significantly depending on donor and recipient surgical approach for living donor kidney transplant. Notably, robotic recipients had equivocal outcomes to the open recipient groups in all measured variables. Further work should study larger cohorts and delineate potential advantages of minimally invasive approaches such as rates of surgical site infections and wound complications.
Long-term Compromised Immune Regulation After Rituximab Induction in Blood Group Incompatible Living-Donor Renal Transplantation - 5 Year Results of a Prospective Pilot Study

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1Department of Internal Medicine, University of Giessen, Giessen, Germany; 2Institute of Immunology, University of Heidelberg, Heidelberg, Germany; 3Transplant Immunology Research Center of Excellence, Koç University, Istanbul, Turkey; 4Institute of Medical Virology, University of Giessen, Giessen, Germany; 5Department of Surgery, University of Giessen, Giessen, Germany.

Background: An increased frequency of severe infectious diseases and BK viremia has been described after ABOi renal transplantation. As rituximab induction may alter immunoregulation in these patients, we analyzed clinically relevant immune parameters in a prospective renal transplant study up to 5 years posttransplant.

Materials and Methods: Mononuclear cell subsets (peripheral blood; lymph nodes taken during transplant surgery), intracellular cytokine responses, CD4 helper function and in-vitro B cell responses were assessed pretransplant and up to 5 years posttransplant in 85 renal transplant recipients (living donation: n=25 ABO incompatible (ABOi) and n=30 ABO compatible (ABOc); deceased donation (DD): n=30, all ABO compatible).

Results: Severe infectious diseases occurred more often in ABOi than ABOc recipients within 2 years posttransplant (11/24 (46%) versus 6/30 (20%), P=0.042) but not beyond. The incidence of BK viremia was significantly enhanced in rituximab versus non-rituximab treated patients (1 year: 9/29 (31%) versus 4/54 (7%), P=0.009; 5 years: 10/30 (33%) versus 7/53 (13%), P=0.029). After rituximab induction in ABOi recipients, counts of peripheral blood B cell subsets were profoundly downregulated even 3 years posttransplant and reached the level of non-ABOi recipients after 4 years (memory B cells after 5 years). T-dependent and T-independent B cell responses were significantly impaired in ABOi patients up to 2 years posttransplant (P=0.010 and P=0.053, respectively) whereas CD4 helper activity was not compromised. CD4+ T cell counts were significantly lower in ABOi compared to ABOc recipients at 3 and 6 months (P=0.025 and P=0.046, respectively), but showed no differences in the percentage of Tregs. In regional lymph nodes of ABOi patients, we found a significant downregulation of CD20+ but not CD19+ B cells (P<0.0005), of naive B cells (P=0.031) and short lived plasma cells (P<0.0005) at the time of transplantation.

Conclusion: An increased frequency of severe infectious diseases and BK viremia in rituximab treated ABOi renal transplant recipients may be explained by significantly downregulated CD4+ T cell counts up to 6 months and a profoundly delayed B cell repopulation, most pronounced with regard to memory B cells, together with compromised B cell responses up to 2 years posttransplant. IL-10, as a key player in chronic BK virus infection, was not upregulated in rituximab-treated ABOi transplant recipients.
423.12

Dietary Protein Intake and Blood Pressure After Living Kidney Donation

Ekamol Tantisattamo1, Natchaya Polpichai2, Watthanon Pangkaran3, Phuwadith Wattanachayakul4, Chawin Lopipisuth5, Pakin Lalitnithi5, Pornthira Mutrangura6, Manasawee Tanariyakul6.

1Division of Nephrology, Hypertension and Kidney Transplantation, Department of Medicine, University of California Irvine School of Medicine, Orange, CA, United States; 2Faculty of Medicine Songklanagarin Hospital, Prince of Songkla University, Songkhla, Thailand; 3Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand; 4Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand; 5Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Bangkok, Thailand; 6Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Background: High dietary protein intake is associated with worsening kidney function especially in at-risk patients such as living kidney donors; high blood pressure is a known risk factor for kidney disease. Whether pre-donation protein intake contributes to post-donation blood pressure is unknown.

Methods: A single-center cohort study included living kidney donors undergoing living kidney donation in 2021 and divided the patients into 2 groups: low and high pre-donation protein intake defined by dietary protein intake estimated from 24-hour urine collection <1 (LPI) and ≥1 (HPI) g/kg/day, respectively. Association between dietary protein intake and systolic blood pressure during the first two weeks post-donation was evaluated by multiple linear regression.

Results: Of 14 living kidney donors, mean±SD was 44±12 and 50% were female. Half of the study population were in the LPI group with a mean dietary protein intake of 0.8±0.1 g/kg/day and the remaining seven patients in the HPI group had a dietary protein intake of 2.2±2.5 g/kg/day (mean difference HPI vs LPI 1.4; p 0.172; 95%CI -0.7, 3.5). Dietary sodium intake was not different between the two groups (mean sodium intake of LPI 3,171±1,315 and of HPI 4,058±1,135 g/day, mean difference HPI vs LPI 887; p 0.202; 95%CI -544, 2,318; Figure 1). Mean systolic blood pressure of LPI and HPI groups were 135±8 and 121±7 mmHg, respectively (mean difference LPI vs HPI 14; p 0.007; 95%CI 5, 23). Compared to the LPI group, the HPI group had 14 mmHg lower systolic blood pressure (β -14; p 0.007; 95%CI -23, -5; Figure 2). After adjusted by age, gender, ethnicity, pre-donation body mass index, dietary sodium intake (<4 vs ≥4 g/day), and the interaction term between dietary protein intake and dietary sodium intake, the magnitude and direction of the association between dietary protein intake and systolic blood pressure remain the same (β -13, p 0.043, 95%CI -26, -0.6) and dietary sodium intake did not modify the association (Pinteraction 0.498).

Conclusions: Higher dietary protein intake during pre-donation is inversely associated with SBP level without the effect of dietary sodium intake. Although HPI is associated with adverse kidney outcomes, the protective association between HPI and high blood pressure may involve physiological change after donor nephrectomy and further studies with long-term follow-up are required.
Epidemiology of Cytomegalovirus Infection and Disease in Hematopoietic Stem Cell Transplant Recipients in Selected Countries Outside of North America and Europe: A Systematic Review

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Background: Cytomegalovirus (CMV) is a highly prevalent herpes virus with a seroprevalence higher in South America, Africa, and Asia than in Europe and North America. In hematopoietic stem cell transplant recipients (HSCT), CMV infection is a common opportunistic infection and a major cause of mortality (1). To better understand the epidemiology of CMV infection and disease post-HSCT in selected countries outside of Europe and North America, a systematic review was conducted.

Methods: Observational studies that included HSCT recipients (any age) from 15 selected countries in Asia-Pacific, Latin America, Russia and the Middle East were considered (search period: 01 Jan. 2011 – 21 Jul. 2021). Outcomes of interest were incidence, recurrence rates and risk factors of CMV infection and disease, and CMV-related mortality at any time point. Indexed publications (Ovid® MEDLINE and Embase, Cochrane Database of Systematic Reviews and World Health Organization database Global Index Medicus) were searched, supplemented by pragmatic searches of the grey literature and snowballing of references lists. The protocol was registered in PROSPERO (CRD42020205559).

Results: A total of 63 studies (range: 33 to 10,206 patients), most conducted in adults (≥ 18 years; n=49 studies, 77.8%) and allogeneic HSCT recipients (n=53, 84.1%), were included in the review. In 43 of 54 studies reporting on incidence of CMV infection, within 1 year post-HSCT, estimates were uniformly distributed between 24.8% and 61.2% (Figure 1). Lower estimates were reported in autologous HSCT recipients (5.3%), and younger patients at the time of transplantation (9.3% in adults with a median age of 25 years and 18.6% in patients aged ≤20 years). Higher estimates (range: 69.4% to 88.2%) were found in 8 studies from China and South Korea, most with a follow-up period > 1 year (median: 27 to 54 months in 5 studies) (Figure 2). Incidence of CMV disease following HSCT was below 20%, with estimates uniformly distributed between 0% and 15.7% in allogeneic HSCT. According to 11 studies, reported rates of CMV recurrence ranged between 19.8% and 37.9%. Commonly reported risk factors for CMV infection or disease in HSCT recipients were high-risk CMV serostatus (R+) (hazard ratio [HR]: 2.6 and 3.7, odds ratio [OR]: 2.2 and 5.4), older age of recipients (HR for each additional year: 1.03-1.04), presence of acute or chronic graft versus host disease (HR: 1.1-2.5), haploidentical HSCT (HR: 2.7-6.4), and use of immunosuppressive agents (OR: 5.0-9.3). CMV-related mortality was reported in up to 10% of patients following HSCT (n=30 studies; period of assessment not reported).

Conclusion: Relatively high rates of CMV infection, CMV disease and CMV recurrence were reported post-HSCT, with CMV-related mortality observed in up to 10% of patients. High rates of CMV infection and disease post-HSCT may impact graft outcomes and increase disease burden in patients post-transplantation.

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Temporal and Diversity Characterization of Metagenomic Viral Detection in Kidney Transplant Recipients

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Introduction: Kidney transplant recipients are highly immunosuppressed and thus predisposed to opportunistic infections. Current viral diagnostic methods from plasma detect single pathogens, often by qPCR. However, an unbiased method detecting common viruses with sensitivity and specificity comparable to qPCR would allow comprehensive diagnosis. Quantification of donor-derived cell-free DNA (dd cfDNA) is an established method for diagnosis of allograft rejection. Combining dd cfDNA quantification and pathogen detection into a single sequencing workflow represents an opportunity to diagnose two impactful complications in transplant recipients.

Method: A total of 1980 plasma samples from 256 CTOT-08 study subjects were tested. Whole genome cfDNA sequencing was performed on an Illumina platform. Sequence data along with recipient genotype, were analyzed using a bioinformatics pipeline to calculate the percentage dd cfDNA present. Non-human reads underwent reference-assisted assembly and taxonomic annotation using KrakenUneq which was trained (K-mer values of 16, 21, and 31) on an in-house database of ~12,000 viral genomes. The final predictions were made by applying a majority-wins rule. Read assembly (contig) length and read depth were reported along with the viruses detected.

Results: Of 256 subjects, 230 (89.8%) had ≥1 sample positive for viral detection. Of the 1980 samples tested, 979 (49.4%) had ≥1 viral detection(s) with contig lengths from 32 – 125,199 bp. The number of viruses detected was negatively associated with dd cfDNA values. For every additional virus detected, dd cfDNA values decreased 7.8% (P<0.001, 95% CI: 4%, 11%). The dd cfDNA values skewed higher in samples with no virus detected (Fig. 1). Torque Teno virus (TTV) was the most common detection (25.6%), followed by BK virus (19.8%), cytomegalovirus (8.3%), adenovirus (2.6%), and Epstein Barr virus (2.6%). Other notable viruses detected included human herpesviruses 1, 2, 6A/B, and 7, JC polyoma virus, human polyomavirus 6 and 8, and gammapapillomaviruses 1 and 9. Concordance with qPCR results was 92.5%, with discordant results <350 copies/mL or contig lengths <100 bp. Analysis of temporal patterns demonstrated the prevalence of viral detection peaked early for all viruses, especially TTV, with declines in prevalence through the study (Fig. 2). Detection of BKV and CMV prior to (1 - 30 days) a clinical diagnosis was documented in 12 of 17 and 7 of 11 samples, respectively. The rate of detection after the clinical diagnosis was 21 of 24 and 4 of 6 for BKV and CMV, respectively.

Conclusion: Metagenomic viral detection combined with dd cfDNA quantification demonstrated sensitive detection of a broad range of DNA viruses, including key pathogens, with a strong temporal pattern. Viral detection was negatively correlated with dd cfDNA values and concordance with qPCR was high. Prospective studies are needed to assess the clinical utility of combined metagenomic and dd cfDNA analysis.
Trends of Antibiotic Resistance in E. Coli, Klebsiella Spp., Pseudomonas Aeruginosa and Enterococcus Spp. Urinary Tract Infection in Renal Transplant Recipients From Pakistan Over a Decade

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Introduction: Antimicrobial resistance is a major public threat worldwide. There has been an emergence of multi-drug resistant (MDR) bacterial infections over the last decade. MDR Klebsiella species have become one of the most common nosocomial pathogens in hospitals. In Pakistan, many studies reported a rising trend of resistance to antimicrobials in clinical isolates of Klebsiella species (spp.), E-coli, Pseudomonas aeruginosa and Enterococcus spp. Solid-organ transplant (SOT) recipients are more prone to infections, particularly with MDR organisms due to immunocompromised status, multiple hospital visits, and increased exposure to antibiotics. There is paucity of data on antibiotic susceptibility patterns among renal transplant recipients from Pakistan. This study is conducted to find the trends in antimicrobial resistance patterns among common organisms isolated in the urinary tract over a 10-year period in renal transplant recipients. The aim is to guide the physicians regarding decisions over empirical antimicrobial choices.

Methods: Sindh Institute of Urology and Transplantation (SIUT) is a 700-bedded tertiary care hospital in Karachi, Pakistan. It has had a comprehensive renal transplantation program with more than 6500 transplantations now. A retrospective computerized data review of urine cultures from renal transplant recipients in 2010 and 2020 was conducted. The trend of E.coli, Klebsiella species (spp.) Pseudomonas aeruginosa and Enterococcus spp. were collected. The resistance pattern of amoxicillin-clavulanic acid, ceftriaxone (ceftazidime for Pseudomonas aeruginosa), piperacillin-tazobactam, ciprofloxacin, amikacin, co-trimoxazole, and imipenem were compared over the 10 years period.

Results: A total of 2,088 out of 6,249 (33%) and 2902 out of 8,115 (36%) urine cultures were positive in 2010 and 2020 respectively. The most common organisms isolated and their trend in the last decade is shown in figure 1. Over the decade, E-coli strains become 100% resistant to ciprofloxacin, ceftriaxone resistance has increased to 80%, and imipenem to 11%. In Klebsiella spp. imipenem resistance has increased to 19%. There is no significant change in the resistance pattern among Pseudomonas aeruginosa. Regarding Enterococcus spp. there is a rise in vancomycin resistance over the decade from 13% to 17% (Figure 2).

Conclusion: Resistance to broad-spectrum antimicrobials has been increased with >10% increase in carbapenems resistance over the last 10 years. E-coli has particularly become more resistant over the decade. We are also seeing more vancomycin-resistant enterococcus. The alarming increase in resistance may lead to increased morbidity in renal transplant recipients because we are left with only injectable options. We need a robust stewardship program for judicious use of antimicrobials and better infection control measures to contain increasing resistance.
424.4
The Protection From CMV Infection in Solid Organ Transplants Is Highly Dependent on CMV T-Cell Specific Immunity And Type of Organ Transplant

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Introduction: The CMV specific immune recovery is known to control viral infection and disease. The CMV specific cell-mediated immunity (CMI) and CMV specific humoral immune response (IgG titer and IgG avidity) was explored as candidate biomarker predictive of CMV infection.

Methods: 653 observations from 297 SOT including 103 kidney (K), 60 liver (L), 47 heart (H), 57 Lung (Lu) transplants. The follow-up was 0-400 days after transplant. The following parameters were examined: 1) CMV serostatus before transplant 2) CMV IgG titer 3) CMV IgG avidity 4) CMV-ELISPOT 5) primary (D+/R-) or non-primary (D+/R+) CMV infection 6) CMV viremia. Data were statistically analyzed using ANOVA and linear regression analysis and spline model.

Results: The main findings of the study were: 1) CMV IgG titers and avidity are not predictive biomarker for CMV infection. The CMV IgG titer and IgG avidity levels are comparable either in infected and non-infected patients. 2) CMV viral load is statistically different between infected D+/R- and D+/R+. The viral load in infected D+/R- is 1 Log higher compared to D+/R+ (10^-5 vs 10^-4 respectively) 4) The CMV immune reconstitution is more rapid and efficient in D+/R- compared to D+/R+. 5) D+/R+ and D+/R- Kidney and Lung transplants display a statistically significant lower CMV compared to heart and liver transplants; 6) Kidney and Lung transplants display a similar pattern of immune recovery. 7) The CMV cell mediated immunity biomarker is predictive of infection in all organs with exception of lung transplants.

Conclusions: The study shows a marginal role of humoral immunity in controlling CMV infection. The pattern of CMI immune recovery is highly dependent upon pre-transplant CMV serostatus, type of organ transplant and immunosuppression therapy. High levels of CMV specific cell-mediated immunity correlate with a reduced CMV infection risk in heart, kidney, and liver transplants. A different scenario emerged in lung transplants: high levels of CMV specific cell-mediated immunity correlate with a reduced CMV infection risk in heart, kidney, and liver transplants. A different scenario emerged in lung transplants: high levels of CMV specific cell-mediated immunity correlate with a reduced CMV infection risk in heart, kidney, and liver transplants. A different scenario emerged in lung transplants: high levels of CMV specific cell-mediated immunity correlate with a reduced CMV infection risk in heart, kidney, and liver transplants.

424.5
Renal Transplant Outcomes: Hepatitis C-Infected Donors and Recipients

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Background: There remains a shortage of kidneys available for transplantation. Increasing the utilization of hepatitis C virus infected organs could reduce the supply demand mismatch in organ transplantation. There is little data about long-term HCV renal transplantation outcomes in the era of effective direct-acting antivirals (DAA). It is important to determine precise outcomes of HCV-positive (HCV+) organs that are transplanted into HCV+ recipients (HCV D+/R+) to quantify risk for patients and other stakeholders, especially as HCV+ organ transplantation continues to expand to HCV-negative (HCV-) recipients.

Methods: We performed a retrospective cohort study of all cases of renal transplantation involving HCV+ recipients at a single academic medical center from 2008-2019. Data was extracted from the institutional electronic transplant database. Demographics, time to transplantation, incidence of organ rejection, and mortality data were compared between HCV D+/R+ and HCV D+/R- groups.

Results: We performed a retrospective study of 3781 kidney transplant recipients between 2008 and 2019. Patients were divided according to recipient/donor CMV serology status at the time of transplant. 121 were HCV D+/R- and 46 were HCV D+/R+. Table 1 shows recipient and donor demographics stratified by D/R HCV serology status. Both groups had similar donor mean age and gender distribution. There were slightly more men and older recipients among HCV D+/R+ compared to the HCV D-/R+ group. The follow-up years were similar between both groups. The time to transplant for those who consented to receive an HCV+ kidney from the time of signing the consent was 407 days vs. 1210 days for those who did not consent. (p=0.0001).

Conclusion: The incidence of rejection and mortality were similar between two groups at follow up. In Cox Hazards Model, we found no association between HCV D+/R+ and increasing risk of rejection or mortality (HR=0.79, 95% CI 0.36-1.74, p=0.20 and HR=0.99, 95% CI 0.41-2.4, p=0.20, respectively: Figure 1). Using a multivariate analysis, we found recipient age as the only independent risk factor for mortality (HR =1.08, 95% CI 1.01-1.14, p=0.015).

Table 1.

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The Screening and Treatment of Asymptomatic Bacteriuria do not reduce the incidence of urinary tract infection or pyelonephritis in the first two months after renal transplantation: A randomized controlled trial

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Background: The incidence of asymptomatic bacteriuria (AB) in the first two months after renal transplantation (pRT) is very high. Due to increased immunosuppression and the use of urinary devices, the screening and treatment of AB in this period could reduce the frequency of urinary tract infection (UTI) and pyelonephritis.

Objective: To evaluate the efficacy of AB screening and treatment in reducing the incidence of UTI in the first two months after kidney transplantation.

Methodology: Randomized, single-blind, controlled clinical trial of pRT patients. Urine culture was conducted on the day of bladder catheter removal, week three pRT, and prior to removal of the ureteral catheter. Patients assigned to the intervention group received treatment for AB based on an antibiogram for 5 days. The control group did not receive treatment. The primary outcome was incidence and time to the first episode of UTI and graft pyelonephritis.

Results: 80 patients were included, 40 randomized to each group. The average age was 29.8 years and 33.7% were women. The cause of chronic kidney disease was classified as "unknown" in 88.7% and only 2 patients had Diabetic Nephropathy (1.25%). The source of the kidney donation was mostly from a living donor (86.2%). The frequency of AB in the intervention group was lower than in the control group (17.5 vs 37.5%, p=0.04). The incidence and time to first UTI and pyelonephritis were higher in the intervention group (25 vs 10%, p=0.07 and 15 vs 2.5%, p=0.04) (Figure 1). Also, the number of UTI was higher in the intervention group (5 vs 18, p=0.05) and the frequency of recurrent UTI (17.5 vs 2.5%, p=0.05). The most common isolated bacteria was E. Coli (n=28, 59.5%) and more than half were E. Coli ESBL (n=15). Bacterial resistance did not differ between intervention groups.

Conclusions: The screening and treatment of AB in the first two months pRT does not reduce the incidence of UTI or graft pyelonephritis and probably could increase their frequency. Generalized treatment of AB during the first months after renal transplantation should be avoided. (Clinical Trials identifier: NCT04333602)

Astra Zeneca and AMGEN.
424.7

Epidemiology of Cytomegalovirus Infection and Disease in Solid Organ Transplant Recipients in Selected Countries Outside of North America and Europe: A Systematic Review

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Background: Cytomegalovirus (CMV), a highly prevalent herpes virus worldwide, can lead to a wide range of serious direct and indirect effects in solid organ transplant (SOT) recipients. As the seroprevalence of CMV varies across countries, a systematic review was undertaken to describe the epidemiology of CMV infection and disease in SOT recipients in selected countries outside of North America and Europe.

Methods: Information sources (search period: 01 Jan. 2011 – 21 Jul. 2021) included literature search (Ovid® MEDLINE and Embase, Cochrane Database of Systematic Reviews and World Health Organization database Global Index Medicus), pragmatic searches of the grey literature, and snowballing of references lists. Observational studies that included SOT (any organ type) recipients (any age) from 15 selected countries in Asia-Pacific, Latin America, Russia and the Middle East and reported on the outcomes of interest (incidence of recurrence rates and risk factors of CMV infection and CMV disease, and CMV-related mortality at any time point) were included. The protocol was registered in PROSPERO (CRD42020205559).

Results: A total of 47 studies (range: 18 to 16,368 pts), most (89.4%, n=42) conducted in adults (≥ 18 years), were retained in the review (kidney: n=33 [70.2%]; liver: n=10 [21.3%]; lung: n=1 [2.1%]; mixed SOTs: n=3 [6.4%]). Reported incidence estimates of CMV infection varied greatly, ranging from 5.2% to 79.0%, according to type of organ transplanted (Figure 1) and country (Figure 2). For CMV disease, incidence estimates within one-year post-SOT ranged from 0% to 19%, in 21 of 23 studies, regardless of prevention strategy used or distribution of CMV serostatus in donor and recipients. Two studies conducted in Brazil reported higher incidence estimates of CMV disease: 30.0% in liver recipients and 34.8% in kidney recipients with a high-risk CMV serostatus (D+/R-). Data on recurrence of CMV infection were scarce (n=4 studies) but consistent rates were reported in 3 studies conducted in adults (35.4%, 35.7%, and 41.0%). Commonly reported risk factors for CMV infection or disease in kidney transplant recipients were high-risk CMV serostatus (D+/R-) (hazard ratio [HR]: 2.7-5.4), older age of recipients (HR: 1.02-2.24), and use of immunosuppressive agents (anti-thymocyte globulin, HR 2.90 or mycophelonate sodium, OR 1.67) and antirejection therapies (OR: 4.2-5.7). No data on risk factors in other SOT recipients were found. In 11 studies covering kidney and/or liver transplant recipients, reported CMV-related mortality rates were up to 5.3% (period of assessment not reported).

Conclusion: Heterogeneity in the incidence of CMV infection across organ types and countries outside of North America and Europe was found, despite most studies reporting on adult kidney recipients. High rates of CMV infection, CMV recurrence and CMV disease are likely to impact graft and patient outcomes post-transplantation and may contribute to greater disease burden post-SOT.

This review was funded by Takeda International AG – Singapore Branch. MS has received grants from F2G, Gilead and personal fees from Gilead, Pfizer, Takeda and Roche for work outside of this research. HT institution has received research grants to conduct clinical trials from Novartis, Pfizer, BMS, Natera and Astra Zeneca. He has also received consulting honoraria from Novartis, Pfizer, Takeda, MSD and CareDx. IS is an employee of Takeda Pharmaceuticals India Pvt Ltd. AS and DD are employees of Takeda International AG – Singapore Branch and hold stock options. JC has received grants from Takeda company. Literature retrieval, analysis and medical writing support were provided by Aurore Bergamasco, Camille Goyer, and Yola Moride of Yolarx Consultants and funded by Takeda International AG – Singapore Branch.
Real-World Treatment Patterns and Outcomes For Cytomegalovirus Infection and Disease in Solid Organ Transplant Recipients in Selected Countries Outside North America and Europe: A Systematic Review

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Background: In Europe and North America, ganciclovir (GCV) and valganciclovir (VGCV) constitute the standard of care for the management of cytomegalovirus (CMV) infection and disease in solid organ transplant (SOT) recipients. As practices vary across countries due to differences in access to health care or resources, a systematic review was undertaken to evaluate treatment patterns for CMV infection and disease post-SOT in selected countries outside of Europe and North America and describe related outcomes.

Methods: Information sources (search period: 01 Jan. 2011 – 21 Jul. 2021) included literature search (Ovid® MEDLINE and Embase, Cochrane Database of Systematic Reviews and World Health Organization database Global Index Medicus), pragmatic searches of the grey literature, and snowballing of references lists. Observational studies that included SOT (any organ) recipients (any age) who developed CMV infection or disease in 15 selected countries in Asia-Pacific, Latin America, Russia and the Middle East and reported on the outcomes of interest (treatment patterns for CMV infection and CMV disease, proportion of patients (pts) with resistant and/or refractory CMV including definitions, treatment-related outcomes and adverse events, AEs) were included. The protocol was registered in PROSPERO (CRD42020205559).

Results: A total of 23 studies (18 to 1,620 pts), most (87.0%, n=20) conducted in adults (≥ 18 years), were included (kidney: n=19 [82.6%]; liver: n=3 [13.0%]; mixed SOTs: n=1 [4.3%]). In studies reporting on preventive strategies used for CMV (n=4), similar proportions of pts receiving prophylaxis and pre-emptive therapy were found (45% to 58.7% pts and 41.3% to 56.3% pts, respectively). Intravenous (IV) GCV and VGCV were the preferred first-line (1L) treatments for both prevention (IV GCV: 77.8%-100% pts, VGCV: 44.4%-99.2% pts) and treatment (IV GCV: 77.8%-100% pts) of CMV infection and disease. In 3 studies, the treatment duration for CMV disease was between 12 and 90 days. In pediatric pts who received GCV as pre-emptive therapy after prophylaxis, time to viremia clearance was 3.5 months. Rates of CMV resistance were reported in 3 studies (Figure 1). No data on risk factors for CMV resistance nor on pts with refractory CMV were found. Hematological AEs (i.e., thrombocytopenia, leucopenia, neutropenia, anemia) were reported in up to 25% of pts receiving IV GCV, as prophylaxis or pre-emptive therapy (Figure 1). Data stratified according to treatment strategy were not available.

Conclusion: The conventional 1L treatment for both prevention and treatment of CMV was IV GCV or VGCV. However, as identified studies reported that 1 in 4 pts experience hematological AEs with these therapies, there remains an unmet need for this patient population. Data on the proportion and management of SOT pts with resistant and/or refractory CMV remains scarce in countries outside of Europe and North America.

This review was funded by Takeda International AG – Singapore Branch. JC has received grants from Takeda company. MS has received grants from F2G, Gilead, Merck and personal fees from Gilead, Pfizer, Takeda and Roche for work outside of this research. IS is an employee of Takeda Pharmaceuticals India Pvt Ltd. AS and DD are employees of Takeda International AG – Singapore Branch and hold stock options. HT has received research grants to conduct clinical trials from Novartis, Pfizer, BMS, Natera, and AstraZeneca.

Literature retrieval, analysis and medical writing support were provided by Aurone Bargamasco, Camille Goyer, and Yola Monde of Yolarx Consultants and funded by Takeda International AG – Singapore Branch.
Real-World Treatment Patterns and Outcomes For Cytomegalovirus Infection and Disease in Hematopoietic Stem Cell Transplant Recipients in Selected Countries Outside of North America and Europe: A Systematic Review

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Background: There is a paucity of real-world data on treatments used for cytomegalovirus (CMV) in hematopoietic stem cell transplant (HSCT) recipients, which differ across countries, outside of developed markets. To address this knowledge gap, a systematic review was conducted to evaluate current treatment patterns for CMV infection and disease following HSCT in selected countries outside of North America and Europe and describe related outcomes.

Methods: Information sources (search period: 01 Jan. 2011 – 21 Jul. 2021) included indexed literature (Ovid® MEDLINE and Embase, Cochrane Database of Systematic Reviews and World Health Organization database Global Index Medicus), conference abstracts, pragmatic searches of the grey literature and snowballing of references lists of retained studies. Observational studies of interest included HSCT recipients (any age) who developed CMV infection or disease in 15 selected countries in Asia-Pacific, Latin America, Russia, and the Middle East. Outcomes of interest were treatment patterns for CMV infection and CMV disease, proportion of patients (pts) with resistant and refractory CMV including definitions, treatment-related outcomes and adverse events (AEs). The protocol was registered in PROSPERO (CRD42020205559).

Results: Out of 25 retained studies (33 to 475 pts), most included allogeneic HSCT recipients (n=21, 84.0%) and adult pts (n=20, 80.0%). In HSCT recipients, pre-emptive therapy with intravenous ganciclovir (IV GCV) and/or valganciclovir (VGCV) is the conventional first-line (1L) approach for CMV infection prevention, with a median treatment duration of 14-24 days (5 studies). GCV IV was also the conventional treatment for CMV disease (5 studies), with treatment lasting 12-30 days (3 studies). Neutropenia was observed in 30.0% and 39.8% pts treated with GCV and, in 3 studies, neutropenia, myelosuppression, and nephrotoxicity led to GCV discontinuation, respectively, in 13.6%, 10.0%, and 2.3% of pts. In 3 studies, up to 10.0% of pts had second-line (2L) treatment with foscarnet, due to GCV-related myelosuppression. The reported proportion of pts with resistant CMV (definition not specified) ranged between 0% and 7.7% (5 studies; Figure 1). These pts received foscarnet or cidofovir as 2L therapy for a mean duration of 14 days (no data on AEs reported). In 3 studies, estimates of refractory CMV were 2.9%, 13.0%, and 49.4% (latter estimate reported in 39 pts, of whom 56.0% had recurrent CMV).

Conclusion: In selected countries outside of North America and Europe, conventional therapeutic options for pre-emptive and treatment of CMV infection and CMV disease following HSCT were IV GCV and VGCV. However, premature treatment discontinuation occurred in up to 1 in 8 pts, highlighting an unmet need with current standard of care. Real-world outcomes in pts with refractory CMV (with or without resistance) were scarce and warrants further investigation in this patient population, including therapeutic management.

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Prediction Model With Quantiferon-CMV for Clinically Significant Cytomegalovirus Event in Seropositive Kidney Transplant Recipients

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Cytomegalovirus (CMV) disease prevention after kidney transplant (KT) is costly, myelotoxic (universal prophylaxis) and requires a complex logistic routine (preemptive therapy). Quantiferon-CMV (QFCMV) is a simple and commercially available test to assess CMV-specific cellular immunity but has not been widely adopted in clinical practice for risk stratification. In this prospective cohort study, we tested the association of QFCMV and clinical variables with the occurrence of a first clinically significant CMV event (CMV disease or asymptomatic viremia above cutoff for preemptive therapy) in the first year after KT. Logistic regressions were employed to build a prediction model. The cohort comprised 100 KT recipients (mean age 51y, 67% male); all patients were adult, CMV IgG positive (R+), received basiliximab as induction therapy and were maintained on prednisone/mycophenolate/tacrolimus. CMV surveillance with qPCR and pp65 antigenemia was employed weekly until day 98 and then bi-weekly until day 180. Results: 39 patients developed a CMV event (disease 10, asymptomatic infection 29) at median 54 days post-Tx. Day 30 non-reactive/indet. QFCMV (but not pre-Tx) was associated with the outcome, along with deceased donor, higher donor and recipient age, day 30 CD8+ count and cold ischemic time. A higher QFCMV cutoff for reactivity (>0.6 IU IFN-g/ml) outperformed the original cutoff (>0.2) for CMV protection. The final multiple prediction model incorporated 3 variables: day 30 QFCMV (≤ 0.6 IU/ml), deceased donor and recipient age (>60y). After correction for optimism by bootstrap, performance measures were R2 47%, c-statistic 0.85, and corrected calibration slope 0.84. When at least 2 of the 3 variables were present, the model predicted the outcome with sensitivity 90%, specificity 72%, negative predictive value 92%; 48% patients were under this probability threshold. In intermediate-risk kidney recipients (R+, non-ATG), a simple clinical prediction model including day 30 QFCMV identified patients who could be spared from CMV prevention measures. The model requires external validation.
A 5-Dose IVIG Protocol Decreases the Risk of Reinfection in Solid Organ Transplant Patients With Secondary Antibody Immunodeficiency: Results of a Multicenter Randomized Clinical Trial

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Introduction: Infection is a leading cause of morbidity and health spending after solid organ transplantation (SOT). Secondary antibody deficiency (SAD), defined as IgG hypogammaglobulinemia, is frequently observed after SOT. In single center, multicenter and metaanalysis, IgG hypogammaglobulinemia has been demonstrated as a risk factor of severe infection in all SOT. Reinfection is more common among patients with SAD after SOT. Intravenous immunoglobulins (IVIG) are used for replacement therapy in primary and secondary immunodeficiencies. In primary immunodeficiency the protocols are well established. However, in SAD, the doses, number of doses and, above all, the time of therapy are not well defined. In a multicenter randomized clinical trial we evaluated the safety and efficacy of a 5-dose IVIG protocol to decrease the rate of reinfection in SOT with severe infections and SAD.

Materials and Methods: Distribution: Heart 20, Lung 15, Kidney 5, Liver transplantation 4 were randomized. Patients with post transplant severe infections and SAD (IgG < 600 mg/dL) were included. IVIG protocol: Two doses of 15 grams (interval between doses 7-15 days) followed by another 3 doses of 20 grams (interval between doses 15-30 days) of a 5% IVIG product. 39 patients that completed the protocol were analysed [IVIG in combination with conventional antimicrobial therapy (n=21) versus conventional antimicrobial therapy alone (n=18)]. Specific antibodies were tested at inclusion in the clinical trial (visit 1, V1) and 30-45 days after last IVIG dose (last-visit, V7) in a subgroup of patients performed at the coordinating center in Madrid (Gregorio Marañon Hospital).

Results: The primary outcome measure (rate of reinfection) was lower in patients randomized to receive IVIG as compared with patients receiving only conventional antimicrobial therapy (28.6 vs 66.7%, chi-square test, p=0.017). Reconstitution of IgG between V1 and V7 was higher in IVIG group as compared with non IVIG group (361±223 vs 255±275 mg/dL, p=0.038). Higher levels of specific IgG anti-cytomegalovirus, IgG antclostridium difficile toxins A and B and IgG1 anti-tetanus toxoid antibodies was demonstrated at V7 in IVIG-recipients as compared with patients that were treated with antimicrobial therapy alone. A significant increase of specific antibodies between V1 and V7 was only observed in IVIG group. A significant decrease of serum BAFF levels was demonstrated in IVIG group. 16 SAE were reported in 13 patients (6/21 IVIG treated patients (28.57%) and 7/18 non-IVIG patients (38.88%), p=0.496). None of SAE was considered to be related with study drug.

Conclusions: We have demonstrated that IVIG is associated with lower rate of reinfection in SOT with severe infection and SAD. Reconstitution of specific antibodies and immunemodulation of serum BAFF was only observed in IVIG-treated patients. We believe that this way of administering IVIG can be validated in future clinical trials with a larger number of patients.
Donor-Derived Acute Hepatitis A Virus Infection in Two Kidney Transplant Recipients From a Common Donor

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Background: Donor-derived hepatitis A virus (HAV) transmission is rarely reported following kidney transplantation. We describe two patients who contracted acute HAV following deceased-donor kidney transplant (DDKT) from a shared donor.

Methods: The donor was a 36 year old woman who died of complications of hepatic encephalopathy. Her history included cirrhosis due to chronic hepatitis C virus (HCV) infection, injection drug use, and alcohol dependence. KDPI was 83%. Donor testing revealed a positive anti-HAV IgG, negative HCV nucleic acid testing, and a positive anti-HAV IgM. The anti-HAV IgM was a clinical test and not included in the donor summary. A 52-year-old man (patient A) and a 48-year-old man (patient B) both underwent DDKT from this donor. Both patients received alemtuzumab induction and immunosuppression, with prior immunity. ALT and TB normalized by 5 months post-transplant, accompanied by nausea, weakness, and malaise requiring hospitalization. Transaminases peaked with alanine transaminase (ALT) 893 IU/L and total bilirubin (TB) 2.4 mg/dL. Liver biopsy showed portal and lobular hepatitis with plasma cell-rich inflammation. Serologic testing revealed a positive anti-HAV IgM, despite pre-transplant testing with anti-HAV IgG positivity consistent with prior immunity; ALT and TB normalized by 5 months post-transplant with supportive care. Patient B had an asymptomatic ALT elevation of 99 IU/L at 3 months post-transplant. He presented to clinic 2 weeks later with jaundice; testing showed TB 6.9 mg/dL and ALT 149 IU/L. Anti-HAV IgM was newly positive; anti-HAV IgG and IgM were negative pre-transplant. His transaminases gradually normalized with supportive care.

Results: This is the second known case of donor-derived transmission of HAV to dual recipients following DDKT. HAV is normally transmitted by the fecal-oral route after contact with infected individuals or with contaminated water or food. Although hepatitis A is usually self-limited, fulminant hepatitis is an uncommon life-threatening complication. HAV is less common in the United States than in developing countries, but outbreaks occur in areas with low vaccination rates. Hepatitis A vaccination is highly protective and is recommended for children and high-risk adults, including travelers to endemic areas and individuals with chronic liver disease. The American Society of Transplantation recommends HAV vaccination for transplant candidates.

Conclusions: Donor-derived HAV infection is rare, but may be under-diagnosed. While active HAV is typically a self-limited disease, transplant recipients may face greater risks. Vaccination reduces the risk of infection and should be considered prior to transplant in non-immune candidates. In transplant recipients presenting with new transaminase elevations, HAV infection should be included in the differential, regardless of pre-transplant immunity.

The Diagnosis and Treatment of Posttransplant Lymphoproliferative Disorder in Pediatric Liver Transplant Recipients

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Objective: To summarize the incidence, diagnosis and treatment experience of posttransplant lymphoproliferative diseases (PTLD) in the pediatric liver transplant recipients.

Methods: We retrospectively analyzed the clinical data of pediatric liver transplant recipients. The incidence, clinical symptoms, laboratory and imaging data of PTLD in pediatric liver transplant recipients were collected. The pathological results and treatment methods were analyzed. The prognosis was evaluated.

Results: A total of 749 pediatric liver transplantation patients were treated at Beijing Friendship Hospital from June 2013 to July 2021, and PTLD was confirmed in 45 patients (9.422.2%, male: 817.8%, donation after death), the incidence of PTLD was 6.0% (45/749) in children after liver transplantation. The median age of PTLD patients was 10.3 months (range, 4.6-146.7 mo). The median time for EBV DNA replication was 2.9 months (range, 0.9-35.1 mo) after the operation, and the median time of onset was 14.6 months (range, 1.2-46.5 mo) after the operation. 90.2% (41/45) of patients with PTLD had superficial lymphadenopathy. Pathological results of 93.3% (42/45) patients showed positive EBER by in situ hybridization. In 43 patients, positron emission computed tomography (PET)-CT revealed increased FDG metabolism in the associated enlarged lymph nodes. All 45 patients were treated with reduced immunosuppressive drugs, and some of the patients were treated with targeted therapy, chemotherapy, surgical resection and adoptive immunotherapy depends on its pathological types. Twelve patients were in stable condition, two patients died of progressive disease, and 31 patients achieved complete or partial remission. After treatment with reduction in immunosuppression, rejection occurred in 6 patients, and liver function improved after administration of the immunosuppressive drug.

Conclusions: Primary EBV infection and immunosuppression after liver transplantation in children may increase the risk of PTLD. The possibility of PTLD should be considered in nonspecific symptoms with increasing EBV DNA load and superficial lymphadenopathy. Monitoring EBV DNA replication load and decreasing immunosuppression are essential methods to treat PTLD in children after liver transplantation. However, after reducing the level of immunosuppression, we should pay close attention to the liver function and guard against rejection. Key words: Pediatric Liver transplantation; Posttransplant lymphoproliferative disease; Epstein-Barr virus infection; reduction in immunosuppression.
Single Cell Alloreactive TCR Repertoire Profiling

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Aims: We discovered >40 K b-peptide epitopes directly recognised by alloreactive CD8 T cells from B10.BR mice (H-2 k). Here, we integrated two approaches to profile the alloreactive T cell repertoire at an early stage in tolerance induction (Fig. 1a).

Methods: B10.BR mice were primed with a K b-expressing skin graft followed by inoculation with AAV-K b. Nested PCR and Sanger sequencing of paired αβ TCR from single dextramer-positive cells was performed in parallel with BD Rhapsody library preparation/Illumina sequencing for paired TCR and targeted transcriptome analysis.

Results: Repertoires for 3 dominant epitopes (K b-SNY, K b-RTY and K b-VGP) were determined (Fig. 1b). TCR αβ diversity was significantly reduced among epitope-specific T cells (scores K b-SNY 47.3, K b-RTY 69.5, K b-VGP 279.5) compared with PD-1 neg bystander cells (score 78730). Alloreactive repertoires were strongly skewed towards usage of particular V-J gene segments and comprised families of related TCRs including both private TCR clones and public meta-clonotypes (Fig. 1b-d). One cross-reactive clone recognised both K b-SNY and K b-RTY (Fig. 1c-d). A number of clones shared the same b chain paired with different alpha chains (Fig. 1d) while clones with dual alpha chains were also detected. The major meta-clonotypes were represented in multiple mice.

Rhapsody analysis of K b-reactive (PD-1 hi), bystander (PD-1 neg) or K b self-tolerant T cells (from the Kb-transgenic H-2k strain 178.3) permitted profiling of a broader range of donor-reactive T cells. Comparison of V gene segment usage across the range of receptors expressed by PD-1 neg cells from Sanger-sequenced or Rhapsody samples (502 or 1151 cells respectively) did not reveal any biases in the repertoire obtained based on the amplification method (Fig. 2a). TRAV14 and TRAV16 were over-represented among the PD-1 neg cells compared to PD-1 neg or Kb-tolerant cells while cells expressing TRAV9 and TRAV12 were less frequent (Fig. 2b). The top 10 clones from each mouse accounted for 32% of all K b-reactive (PD-1 hi) cells. No clonal expansions were observed in the PD-1 neg or K b self-tolerant populations, with negligible overlap between TCR sequences from PD-1 hi cells and these populations. K b-reactive cells segregated into clusters corresponding to liver-resident or peripheral memory, precursors exhausted and proliferating cells, while PD-1 neg cells displayed a central memory phenotype (Fig. 2c-d). Individual clonotypes showed distinctive gene expression patterns following activation.

Conclusions: Directly-alloreactive CD8 T cell repertoires comprise families of closely-related clonotypes. Gene expression early during tolerance induction may determine the subsequent fate (deletion/exhaustion) of individual clones.
Recipient Myeloid Cell Myeloperoxidase Is Required for NK Cell Activation and Regulates Antibody-Mediated Acute VS. Chronic Kidney Allograft Rejection

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Acute and chronic antibody-mediated rejection (ABMR) continue to be major problems undermining the success of kidney and other solid organ transplants. Cellular and molecular mechanisms underlying these pathologies remain largely unclear. Dysregulated donor-specific antibody (DSA) responses are induced in B6.CCR5-/- mice transplanted with complete MHC mismatched A/J kidney allografts and are required for rejection of the grafts. Acute ABMR of kidney allografts in B6.CCR5-/- recipients also requires myeloid and NK cell activation to express pro-inflammatory effector functions within the graft. This study tested the role of myeloid cell functions on NK cell activation and on allograft survival during ABMR by using recipients deficient in the myeloid cell-derived enzyme myeloperoxidase (MPO).

A/J kidneys transplanted to B6.CCR5-/- recipients rejected between days 18-25 with histopathology of acute ABMR whereas A/J allograft rejection in B6.CCR5-/-MPO-/- recipients occurred between days 46-54 with histopathological and molecular features of chronic graft injury. On day 15, allograft-infiltrating NK cell activation to proliferate and express CD107a was markedly decreased in B6.CCR5-/-MPO-/- recipients and was accompanied by decreased graft expression of NK cell activation genes, including SH2D1B1, and IFN-g and the monocyte/macrophage chemoattractant CCL2. NanoString analysis of RNA from isolated NK cells infiltrating allografts in CCR5-/- vs. B6.CCR5-/-MPO-/- recipients on day 14 post-transplant indicated completely different transcriptomes, including integrin activation and matrix degradation pathways that were markedly decreased in B6.CCR5-/-MPO-/- recipients and was accompanied by decreased graft expression of NK cell activation genes, including SH2D1B1, and IFN-g and the monocyte/macrophage chemoattractant CCL2. NanoString analysis of RNA from isolated NK cells infiltrating allografts in CCR5-/- vs. B6.CCR5-/-MPO-/- recipients on day 14 post-transplant indicated completely different transcriptomes, including integrin activation and matrix degradation pathways that were markedly decreased in graft infiltrating NK cells in B6.CCR5-/-MPO-/- vs. those infiltrating allografts in CCR5-/- recipients. The phenotype of allograft infiltrating myeloid cells was also altered in B6.CCR5-/-MPO-/- recipients and allograft histopathology on day 14 post-transplant indicated marked decreases in Mac-2+ activated macrophages in grafts from B6.CCR5-/-MPO-/- recipients. NanoString analysis of isolated myeloid cells infiltrating the kidney allografts of the two groups of recipients on day 14 post-transplant also indicated different transcriptomes, including decreased expression of gene pathways involved in phagocytosis, platelet degranulation, and endosomal TLR signaling by myeloid cells infiltrating allografts in B6.CCR5-/-MPO-/- recipients, that correlated with the histopathological change from acute to chronic ABMR. Overall, the results indicate that expression of MPO is required for activation of kidney allograft-infiltrating NK cells and monocytes/macrophages that promote acute AMR of kidney allografts and in the absence of recipient cells producing MPO DSA promotes development of chronic ABMR.

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Single-Cell Immune Profiling of Human Intestinal Allografts Reveals Differential Phenotypes of Alloreactive T-Cell Clones in Quiescent vs Chronically Rejecting Allografts

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Introduction: The success of intestinal transplantation (ITx) is limited by high rejection rates. We have demonstrated that host-vs-graft (HV/G) alloreactive T-cell clones are enriched in intestinal allografts during early rejection and persist despite rejection resolution. Recipient T cells in the mucosa eventually take on resident memory T cell (TRM) features, possibly posing a constant threat of late rejection.

Methods: We integrated clonotype, alloreactivity and gene expression profiles of FACS-sorted allograft recipient T cells to assess the functional phenotype of donor-reactive mucosal T cells in association with graft outcomes using the 10x single cell RNA sequencing platform and our method for identifying donor-reactive TCRs from pre- and post-Tx mixed lymphocyte reactions (MLRs) (Fig.1A).

Results: Recipient mucosal T cells from 6 quiescent and 5 chronically rejecting allograft specimens and a non-transplant control intestine shared at least five transcriptionally-defined clusters (Fig.1B-C): multifunctional (IL17A+, IL22+, TNF+) TRMs (CD69+, ITGAE+, CXCR6+); cytotoxic γδ and CD8 αβ T cells with mixed effector T cell (Teff) and TRM features (CD69dim, RUNX3+, TBX21+, GZMB+); follicular helper T cells (Tfh: CXCR5+, PDCD1+, Bcl6+); nonTRMs (CCR7+, KLF2+, S1PR1+); and regulatory T cells (FOXP3+, CTLA4+). Pre-Tx MLR-defined HV/G clones were mainly detected in TRM, Teff/TRM and Tfh clusters in both quiescent and chronically rejecting allografts. Hyporesponsiveness of circulating recipient T cells to donor vs third-party antigens in post-Tx MLR indicated partial tolerance of circulating recipient T cells to donor antigens post-Tx (Fig.1D). There was a significantly decreased likelihood of detecting HV/G clones defined by post- compared to pre-Tx MLR in late quiescent (but not chronically rejecting) allografts (Fig.1E). Quiescent allografts contained a significantly greater percentage of pre-Tx HV/G clones that became tolerant in post-Tx MLR in ileum compared to PBMCs (Fig.2A-C). Cells classified as missing HV/G (HV/G in pre-Tx MLR and not detected in post-Tx MLR or circulation) and de novo HV/G (unmappable in pre-Tx MLR and unstimulated cells but HV/G in post-Tx MLR) in chronically rejecting allografts showed significantly higher expression of genes related to cytotoxic Teff functions compared to those in quiescent allografts (Fig.2F).

Conclusion: Single cell immune profiling reveals distinct contributions of pre-existing HV/G-reactive T cells that potentially became tolerant in allografts with TRM transcriptional profiles in quiescent vs chronically rejecting allografts.
425.4

The Role of Role of Sex and T Cells in Natural vs Induced ABO Antibody Production in Mice

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Introduction: Interaction of ‘natural’ ABO antibodies (nAbs) with their cognate AB(H)-antigens (Aggs) poses a high risk of rapid rejection of ABO-incompatible (ABOi) organ transplants. We previously demonstrated that a clear understanding of factors influencing ABO nAbs is crucial for successful ABOi heart transplantation. Here we investigated anti-A nAbs vs. intentionally.

Methods: Adult wild-type (WT) and CD4 T cell knock-out (CD4KO) mice (C57BL/6 (B6) background) received weekly i.p. injection x3 of human ABO-A blood cell membranes (Hu-A BCM; 100ul of 10% v/v) or left untreated. Serum anti-A Ab was measured by hemagglutination assay using ABO-A erythrocytes from our A-transgenic mouse line. To test for T cell help and/or suppression, sex-matched CD4+ T cells (8-12x10^6/mouse) or CD4+CD25+ T cells (1.7-2.8x10^6/mouse) from spleens of WT mice were transferred to CD4KO mice. After adoptive transfer, CD4+ T cell reconstitution in peripheral blood was confirmed and mice were left untreated or challenged with Hu-A BCM and assessed for anti-A Ab.

Results: In contrast to WT mice, untreated CD4KO females produced dramatically more anti-A than males, rising substantially with puberty, and this was significantly suppressed in both sexes by adoptive transfer of sex-matched CD4+ T cells. Unlike WT mice, attempted sensitization of CD4KO mice with Hu-A BCM failed to induce additional anti-A beyond the already high levels in either sex; CD4+ T cell adoptive transfer rendered CD4KO mice responsive to A-sensitization. CD4+CD25+ T cell transfer into CD4KO mice neither suppressed anti-A nAbs nor rendered them responsive to A-sensitization (Figure).

Conclusions: When ABO ‘natural’ antibodies are discriminated from intentionally induced Abs, several important findings emerge: 1) Anti-A nAbs are produced without CD4+ T cell help in a sex- and age-dependent manner, suggestive of a role for sex hormones in regulating anti-A nAbs. 2) CD4+ T cells, but not CD4+CD25+ regulatory T cells, down-regulate anti-A nAb production. 3) In contrast to anti-A nAbs, production of anti-A iAbs was CD4+ T cell-dependent without a sex bias.

425.5

Achieving Localized Immunosuppression Through Ex Vivo Engineering of Organ Blood Vessels

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Introduction: Classic immunosuppressants lead to systemic immune shutdown, though necessary to mediate transplant rejection, it may lead to various complications. To reduce off-target immunosuppression while retaining immunosuppression, we propose sensitization of the endothelial lining of vascular transplants ex vivo to achieve localized immunomodulation. The glycoalyx (eGcx), made up of membrane-bound glycoproteins, is of particular interest due to its ability to control cell to cell communication and the activation of immune response through cell recognition. During organ transplantation, inflammation and oxidative damage occurs and can lead to the shedding and damage of the eGcx layer; this has been linked to organ failure and rejection. We developed an enzymatic approach to modify the surface of the endothelium with immunosuppressive polymers to induce immunomodulatory effects locally. We tested the efficacy of this approach in murine transplants.

Method: We developed a method using tissue transglutaminase (TGase) as the surface immobilizing enzyme and polyglycerol polymers containing sialic acid or sulfate moieties that is compatible with UW organ preservation solution at 4°C. In vitro mechanistic studies were performed using EaHy.926 cells modified with the shedding and damage of the eGcx layer; this has been linked to organ failure and rejection. We developed an enzymatic approach to modify the surface of the endothelium with immunosuppressive polymers to induce immunomodulatory effects locally. We tested the efficacy of this approach in murine transplants.

Results: In vitro, polymer modified endothelial cells were able to evade CAR-T cell induced cytotoxicity and reduced oxidative stress. Moreover, polymer treatment reduced TNF release in M1 macrophages. In vivo, modified grafts showed reduced medial thickening and leukocyte infiltration in vessel transplants; further confirmed in the reduction of pro-inflammatory cytokines in serum. In 42 day studies, donor-specific antibody was reduced in polymer-treated grafts compared to untreated. Finally, histological analysis of polymer-treated renal grafts revealed less infiltration and mesangial expansion relating to a healthier graft after 30 days.

Conclusion: Here, the use of a polymer-mediated organ engineering approach leads to vascular protection that prevents immune-mediated rejection of organ transplants. Ex-vivo delivery of these immune cloaking polymers that engineer the blood vessel lumen allow for localized immune protection, making this an enticing and viable strategy for the reduction in the use of broad-active immunosuppressants post-transplantation. The protocol remains simple and easy to deploy, thereby enhancing its potential clinical applicability. To further validate this novel approach, studies in larger animal models that more closely replicate human transplant conditions are being planned.

Recognition of Donor MHC I Disrupts Recipient Reparative Macrophage Differentiation

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Introduction: After tissue injury, infiltrating monocytes differentiate into CD86hiLy6chi pro-inflammatory and CD206+CD301+ reparative macrophages (MΦs) that complete repair. MΦs differentiation is coordinated by tissue injury signals, often referred to as damage-associated molecular patterns (DAMPs), and local cytokines. For example, after heart transplant (HTx) IL-33 is released from graft fibroblasts and acts as a reparative/regulatory DAMP that metabolically reprograms MΦs to differentiate into reparative subsets that protect against chronic HTx rejection. Transplanting allogeneic materials is a novel situation where innate allorecognition of mismatched MHC may disrupt normal MΦ responses to damaged tissues. For instance, paired immunoglobulin-like receptor (PIR)-A3 on C57BL/6 (B6) monocytes recognition of BALB/c H2-Dd triggers their differentiation into pro-inflammatory dendritic cells that promotes HTx rejection. Monocyte PIR-B binding to self MHC negatively regulates PIR-A signals. How PIRs shapes DAMP-mediated MΦ differentiation after Tx is not understood, so we hypothesize that in addition to DAMPs, recognition of self versus allogeneic MHC by PIRs modulates reparative or inflammatory MΦ differentiation.

Methods: Monocyte-derived MΦ differentiation in response to donor materials was tested by administration of 20x10⁶ irradiated BALB/c allogeneic (H-2d; Allo) or (B6) syngeneic (H-2b; Syn) splenocytes intraperitoneally alone or with recombinant IL-33. Recipients of donor cellular materials were B6 wildtype (WT), Rag2−/-γc−/-, Pira−/- and Pirb−/- mice. The precise impact of H-2Dd (Allo) or H-2D b (Syn) recombinant MHCI on MΦ differentiation was determined using B6 WT and Pira−/- bone marrow-derived MΦs (BMDMs). Flow cytometry was utilized to assess MΦ differentiation.

Results: Administration of Syn cells predominantly stimulated monocyte differentiation into CD206+CD301+ reparative and CD206+CD301+ reparative macrophages (MΦs) that complete repair. MΦs differentiation is coordinated by tissue injury signals, often referred to as damage-associated molecular patterns (DAMPs), and local cytokines. For example, after heart transplant (HTx) IL-33 is released from graft fibroblasts and acts as a reparative/regulatory DAMP that metabolically reprograms MΦs to differentiate into reparative subsets that protect against chronic HTx rejection. Transplanting allogeneic materials is a novel situation where innate allorecognition of mismatched MHC may disrupt normal MΦ responses to damaged tissues. For instance, paired immunoglobulin-like receptor (PIR)-A3 on C57BL/6 (B6) monocytes recognition of BALB/c H2-Dd triggers their differentiation into pro-inflammatory dendritic cells that promotes HTx rejection. Monocyte PIR-B binding to self MHC negatively regulates PIR-A signals. How PIRs shapes DAMP-mediated MΦ differentiation after Tx is not understood, so we hypothesize that in addition to DAMPs, recognition of self versus allogeneic MHC by PIRs modulates reparative or inflammatory MΦ differentiation.

Conclusions: These data indicate allorecognition by monocytes or MΦs disrupts the typical generation of reparative MΦs in response to injury. We show that monocyte-derived MΦs PIR-B recognition of self MHC may trigger expression of the receptor needed for IL-33-mediated reparative MΦ differentiation. These new data provide important insights into how innate allorecognition and repair pathways intersect to direct the differentiation of reparative or inflammatory MΦs that shape HTx outcomes.

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Dyslipidemia in Kidney Transplant Recipients: Is It Time for A Change in Strategy?

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Introduction: Dyslipidemia is common in kidney transplant recipients (KTRs), and is associated with a more than 20-fold higher risk of major adverse cardiovascular events compared to the general population. Although KDIGO 2013 guidelines suggest that all KTRs be treated with statins, they are poorly tolerated due to myopathy, hepatotoxicity, and interaction with immunosuppression medications leading to poor compliance. The introduction of the novel lipid-lowering Proprotein convertase subtilisin/Kexin type 9 (PCSK-9) inhibitors presents an opportunity to treat a significant unmet need in KTRs.

Methods: Here we report findings of 3 studies related to hyperlipidemia in KTRs. We conducted a single-center cross-sectional analysis of 250 KTRs about the prevalence of hyperlipidemia, ASCVD scores, frequency of lipid monitoring, and statin use. After our analysis, we performed a nationwide survey using a questionnaire on a lipid management strategy that was sent out to KTR providers and pharmacists. We also conducted a prospective study evaluating PCSK-9 inhibitor (Evolocumab) in the treatment of LDL-cholesterol (LDL-C) levels for KTRs. Patients included in the study were started on Evolocumab 140mg subcutaneously every 2 weeks and their lipids were checked at 3 months.

Results: Our institutional study showed suboptimal lipid control in KTRs with only about 52.3% getting optimal monitoring (Figure 2). This was also seen in the national survey involving 34 centers, where we found disparities and a lack of general consensus in lipid management (Figure 3). With regards to PCSK-9 inhibitor study, all 17 patients with 3 monthly follow-up (n=44 enrolled to date) showed a significant drop in their LDL-C levels (35% to 90%). There was also a remarkable reduction in ASCVD scores. The mean eGFR for all patients was stable (Figure 4). Overall, Evolocumab was well tolerated by all patients.

Discussion: Sub-optimal lipid control found at our institution, along with the disparities in the survey responses indicate that there is no uniform strategy in lipid management in KTRs. This could be due to a lack of strong evidence on which the 2013 KDIGO guidelines are based. There is a need for long-term studies to assess the benefits of lipid management on patient and graft survival in KTRs and the development of a clearer, more standardized approach to the management of lipids. In terms of treatment, PCSK-9 inhibitors appear to be very effective for the reduction of LDL-C levels in KTRs. They have a favorable side effect profile and do not interact with immunosuppressive medications. Unlike cardiovascular benefits shown by statins in long-term studies, there is no data regarding PCSK-9 inhibitors as of yet. Given the challenges faced with statins, PCSK-9 inhibitors could be considered the therapy of choice for statin-intolerant patients, if supported by evidence of beneficial cardiovascular outcomes.

“Study of safety and efficacy of PCSK-9 inhibitor (Evolocumab) in kidney transplant recipients.” is funded by AMGEN.
The Impact of Donor Body Mass Index on Graft Survival After Living Kidney Transplantation

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Introduction: As the obesity epidemic worsens, kidney transplant (KT) candidates are also more obese as well as their potential living and deceased donors (DD). Increased scarcity of organs makes it necessary to adjust the acceptance criteria and has led to the acceptance of living donors (LD) that were previously declined. Many studies found that donor and recipient obesity are significantly related to a decreased graft and patient survival on both living and DD kidney transplant. We aimed to investigate the impact of donor body mass index (BMI) on graft in a cohort of recipients of living kidney transplant (LKT).

Methods: This is a unicenter retrospective observational study that included LKT between 2008 and 2017. Several clinical data were analyzed as depicted in table 1, including the number of acute rejections at the first year, and the graft glomerular filtration rate (eGFR) during the follow-up time (CKD-EPI equation). We grouped donors based on their calculated BMI as follows: <25, 25–30, > 30 kg/m². The Kaplan-Meier curves and Cox proportional hazards regression were used for survival analysis and linear mixed regression was used to evaluate the slope of recipient eGFR over time, according to BMI groups.

Results: We observed 210 LKT. Mean follow up time was 5.2±2.8yeras. The mean age of recipients and donors was 41.3±13.3 and 48.0±10.6, respectively. Thirty percent of recipients and 72% of donors were female. Donors had a mean BMI of 25.3±3.5kg/m². The mean eGFR among donors was 100.1±14.2 at the time of donation. Table 1 shows immunological features of the transplant. Censored graft survival rate at 8-years after transplantation was 92%, 84%, and 40% in recipients from donors BMI <25, 25–30 and >30, respectively. Overall graft survival at 8-years after KT was 92%, 79%, and 40% in BMI <25, 25-50 and ≥30, respectively (figure 2). BMI ≥30 (OR= 4.475; p=,035 vs BMI <25) was an independent predictor of censored graft survival in a multivariate analysis, besides acute rejection at 1-y (OR=3.639; p=,037), although none was statistical significant when global graft survival was considered. Comparing with donor BMI <25 kg/m², a higher donor BMI was associated with a steeper annual decline in eGFR slope after one year after transplantation which difference were -1.0 [95% CI (-1.7)-(-0.3), p=,005] and -2.5 [(-3.9)-(-1.1), p<0.001], among donors with a BMI 25-30 and ≥30 kg/m², respectively, compared to not overweight donors.

Conclusion: Donor obesity had an adverse impact on graft outcome after LKT in our population. This study also shows that slope in eGFR was superior in recipients of overweight donors (OD) in LKT. The selection of living OD must be careful because outcomes in this population seem worse, particularly for the obese. Further studies are necessary to establish adequate BMI cutoffs, that may help the decision for transplant professionals.
Background: Obesity among kidney transplant (KT) recipients can lead to metabolic comorbidity-associated deaths. This study compares post-KT survival between obese and non-obese patients and outcomes of living donor (LD) and deceased donor (DD) grafts.

Methods: Between 1/2005-5/2019, 1403 KT recipients from a single center were included in the study, 314 patients (22.4%) with obesity (BMI>30 kg/m²) in the study group, and 1089 (77.6%) in the control group (BMI≤30 kg/m²). Kaplan-Meier method was used for survival analysis and Cox regression was used to identify risk factors for graft loss and mortality. Propensity score matching analysis adjusting for age, IHD, and T2DM was performed.

Results: The study group had a higher incidence of obesity related comorbidities, delayed graft function and primary non functional (p<0.001). One-, 5-, and 10-year patient survival rates were 96.0%, 87.7%, and 68.3% for the study group and 98.0%, 93.6%, and 80.5% for control group (p<0.001). The respective 1-, 5-, and 10-year graft survival rates were 91.7%, 79.7%, and 58.6% for the study group and 95.4%, 87.3%, and 71.0% for the control group (p<0.001).

Conclusions: Recipient age and metabolic comorbidities should be emphasized when evaluating patients with obesity. We suggest considering LD sizing when evaluating patients with obesity. We suggest considering LD transplantation in this population since it does not show an increased risk for graft loss.

The Gut Microbiome Facilitates Metabolic Syndrome (MBS) Post Kidney Transplantation

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Introduction: Death with kidney allograft function remains a challenge due to the propensity of kidney transplant recipients (KTRs) towards cardiovascular comorbidities including the metabolic syndrome (MBS). This is in spite of efforts to modify these risks via immunosuppressive management and steroid avoidance. Dysbiosis of the gut microbiome impacts lipid metabolism, insulin resistance and atherosclerotic factors. Gut dysbiosis has been demonstrated in KTRs with possible links to the alloimmune response. We hypothesized that changes in gut microbiome pre- and post-transplant may contribute to the development of MBS in KTRs.

Methods: We prospectively collected stool specimens from 14 consecutive patients with End Stage Kidney Disease prior to receiving a living donor kidney transplant (pre-Tx), with a second collection at 6-12 months post-transplant (post-Tx). Eight healthy controls provided specimens for comparison. Demographics and clinical variables were extracted from the electronic medical record. Stool was analyzed for 16S rRNA gene sequencing, microbial metagenome analysis, and targeted and untargeted metabolomics. We measured 69 gut metabolites in serum (GC-TOFMS with a XCF [methyl and ethyl chlorofomate] deviation method) and 104 fecal metabolites (LC-MS measures of bile salt and other metabolites). The primary outcomes were differences in the microbiome and metabolome of KTRs pre-Tx vs control and vs post-Tx. Secondary outcomes were microbiome and metabolome differences between pre-Tx versus post-Tx stratified by MBS status and if a microbiome or metabolome “signature” predicted MBS outcome in KTR.

Results: 11 KTRs met criteria for MBS pre-Tx, of which 8 were stable or worsened MBS and 3 improved MBS post-Tx. 1 patient developed MBS de novo. Compared to controls, pre-Tx microbiome were less diverse, had increased E.coli and Fusobacterium and less Coprococcus and Roseburia, had higher OKD metabolites, lower short chain fatty acids, and higher glutathione (oxidative stress) and proteolytic metabolic pathways. Post-Tx microbiome showed increased Roseburia and decreased Akkermansia, less uremic toxins and less proteolytic pathways. Untargeted metabolomics aligned with improvement in MBS post-Tx (Fig. 1) and independently discriminated between MBS outcomes (Fig. 2). Improved MBS post-Tx was associated with increased Ruminococcus, decreased Akkermansia, and saccharolytic (and butyrogenic and methanogenic) pathways.

Conclusion: Our findings demonstrate that the gut microbiome can clearly discriminate pre- and post-kidney transplant MBS states and also provides a signature for status of MBS post-Tx. These data support efforts to condition the gut microbiome using targeted prebiotics and probiotics to confer a beneficial metabolic state pre-Tx and post-Tx. Gut microbiome manipulation may provide potential adjunct approach to support long term patient and graft survival.
Regular Physical Activity in the Prevention of Post-transplant Diabetes Mellitus and Associated Metabolic Conditions in Kidney Transplant Recipients

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Introduction: Post-transplant diabetes mellitus (PTDM) is significant risk factor for the survival of graft recipients and occurs in 10-30% of patients after kidney transplant (KT). PTDM is associated with premature cardiovascular morbidity and mortality. Insulin resistance (IR) at the time of KT is the most significant risk factor for the development of PTDM in patients after KT, as demonstrated by several analyzes. It is possible to reduce the high incidence of PTDM and affect the long-term survival of patients and grafts by influencing just modifiable risk factors, including obesity and the associated IR. The aim of this work is to determine the effect of regular physical activity on the development of PTDM and its risk factors in patients after KT.

Methods: This was a prospective controlled analysis, which included 44 patients after primary KT in the Martin Transplant Center. Half consisted of a study group (n = 22) whose patients were assigned to perform regular physical activity. The primary goal was to complete at least 150 minutes of moderate intensity physical exertion per week. They performed an aerobic or combined (aerobic + strength) type of sports activity. Monitoring was provided by a sports tracker (Xiaomi Mi Band 4 compatible with Mi Fit mobile application). The other half was made up of a control group. The exclusion criterion at that time was already diagnosed with diabetes mellitus or a pre-diabetic condition. IR was assessed using the HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) index from fasting blood glucose and insulinemia values. Each patient underwent an oral glucose tolerance test (oGTT) at the end of follow-up. Patients in both groups have the same immunosuppressive protocol. The duration of follow-up was 6 months.

Results: We confirmed a statistically significantly higher IR at 6 months (P = 0.0202) and fasting blood glucose at 3 and 6 months (P = 0.0279) by multivariate analysis in the control group (figure 1, 2). After the end of the follow-up, there were significantly fewer patients with normal oGTT in the control group compared to the study group at 6 months (P < 0.0001), significantly more patients with pre-diabetic condition (impaired plasma glucose, impaired glucose tolerance) (P = 0.0078) and diagnosed with PTDM (P = 0.0212) (figure 3). Significantly lower waist circumference at 3 and 6 months (P = 0.0437, P = 0.0372) and low-density lipoprotein at 6 months (P = 0.0444) were found in the study group compared to the control group. In the study group, the subgroup performing intensive training achieved a significant additional effect on the reduction of waist circumference (P = 0.0172). Patients practicing only aerobic activity achieved significant decrease in triglycerides compared to those practicing combined activity (P = 0.046).

Conclusion: In our study, we confirmed a significant effect of regular physical activity in preventing the development of PTDM and associated pre-diabetic conditions.
Prebiotic Supplementation in Kidney Transplant Recipients
For Preventing Infections and Gastrointestinal Upset: A Randomized Controlled Feasibility Study

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Background: Modulating the large intestinal microbiome of kidney transplant recipients (KTR) may reduce infectious complications. The aim of this study was to assess the feasibility of a randomized controlled trial of prebiotics in reducing infections and gastrointestinal symptoms in KTR.

Methods: Acute KTR were recruited to a double-blind, placebo-controlled, randomized trial at the Princess Alexandra Hospital. Patients were provided with prebiotics or placebo for 7 weeks. The primary outcome was feasibility, defined as recruitment of ≥80% of eligible people within 6 months. Secondary outcomes included adherence and tolerability, participant retention in trial, proportions of participants providing serum and stool specimens, self-reported quality of life (QOL), gastrointestinal symptoms and infection events.

Results: During the 7-week period, 72 patients met eligibility criteria, of whom 60 (83%) consented to participate (mean±SD age 53±12 years; 62% males). Fifty six (78%) participants were randomized (27 intervention and 29 control). While participants receiving intervention experienced reduced gastrointestinal symptoms (-0.28 [IQR -0.67 to 0.08] vs -0.07 [IQR -0.27 to 0], p=0.03), both control and intervention groups were similar in adherence (67% vs. 72%, p=0.36), tolerability (56% vs. 62%, p=0.64), QOL (-0.2 [IQR -0.6 to 0] vs. 0.2 [IQR -0.8 to 0], p=0.82) and infection events (33% vs. 34%, p=0.83). Blood and stool samples were collected from ≥90% of participants in both groups.

Conclusions: It is feasible to recruit and retain acute KTR in a randomized placebo-controlled trial examining the effect of prebiotics on infections and gastrointestinal symptoms. This study also showed that prebiotics significantly reduced gastrointestinal symptoms.

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Donor Dendritic Cell Depletion Allows Novel Insights Into the Alloimmune Response Following Murine Composite Tissue and Skin Transplantation

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Background: Cell-based therapies in vascularized composite tissue allotransplantation (VCA) have demonstrated promising results with the potential to modify life-long conventional immunosuppression. Dendritic cells (DCs) promote pro-inflammatory, alloimmune responses. Of particular interest is the role of DCs as antigen-presenting cells and potential tolerogenic effects as immature DCs.

Material and Methods: Diphteria Toxin Receptor (DTR) transgenic or wild-type (WT) donor mice were used to deplete subsets of DCs or APCs respectively in a fully histoincompatible murine hind limb and skin transplant models; prior to procurement, all donors were either treated with diphteria toxin (DT; at -15 hours) or with clodronate (CL; 8 days prior to Tx). DBA/2J mice served as recipients. Study endpoint was on POD 6. Alloimmune response was assessed sequentially; graft survival, intragraft structural and inflammatory changes were tested serially.

Results: The total number of dendritic cells (CD11b-CD11c+ DC) had markedly increased in recipients of skin WT grafts compared to recipients of VCA WT grafts (p<0.0001). The treatment with CL or DT significantly reduced the numbers of maturated and activated DC in the spleen, blood, and LN of mice receiving a skin graft, whereas numbers of CD11b-CD11c+MHCI+ and CD11b-CD11c+CD40+ DC were exclusively reduced in the spleen of VCA recipients after donor pretreatment with DT. cDC 1 subtypes were significantly higher in VCA WT vs. skin WT recipients (p<0.001). Donor pretreatment with DT decreased cDC1 counts only in recipients of VCA grafts (p<0.001).

Luminex analysis revealed significantly higher TNF-alpha serum levels in the VCA WT vs. skin WT group (p<0.01). TNF-beta serum levels were significantly decreased in VCA depletion groups vs VCA WT group (p<0.001). Clinical signs of acute rejection among the VCA groups revealed higher rejection grades in the WT compared to the DC depletion group according to the BANFF criteria (grade III vs. grade II). Additional injection of immature DCs did not show any difference in allograft survival (p=ns).

Conclusion: This is to our knowledge the first systematic study delineating the role of mature and immature DCs tested across and skin transplants. Those data may help explaining split-tolerance phenomenon in VCA while providing a basic concept for the utilization of mature and immature DCs in modifying alloimmune responses in VCA transplants.
Refinement of Hind Limb Allotransplantation in Mice: Introduction of a Novel Anticoagulation Treatment Protocol That Improves Overall Success Rate

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Background: Animal-based research addresses many important questions in reconstructive transplantation. The mouse hind limb transplant model is a highly sophisticated, but powerful research tool. Unfortunately, success of this model is limited due to graft failure mainly because of vascular thrombosis. In consideration of the 3R principle, introduced to improve handling of laboratory animals and ensure quality of data obtained, a novel anticoagulation protocol was used to enhance animal und graft survival.

Methods: A total of fifty murine hind limb transplantations were performed. Animals were assigned to five groups with different anticoagulation regimens. All grafts were flushed with a heparin-saline solution of different concentrations. Recipient and donor animals of two groups received an additional low-molecular-weight heparin (LMWH) injection protocol.

Results: Graft failure due to vascular thrombosis was observed in groups where grafts were flushed with a solution containing 75 IU/cc of heparin and below or using a 50 IU/cc heparin solution in combination with a low dose LMWH injection protocol (p=0.03). Bleeding episodes with lethal outcomes through the osteotomy were significantly higher in groups where solutions with heparin concentrations of 75 IU/cc and above were administered compared to all other groups (p<0.001). Animals treated with a moderate LMWH injection protocol in combination with 50 IU/cc heparin solution for graft flush demonstrated the best outcome with no animal or graft loss and an overall survival of 100% (p<0.0001).

Conclusion: In regards of the 3R principle, this is the first mouse transplant model utilizing an effective anticoagulation protocol to successfully perform a high-demanding microsurgical procedure.
Military Veterans’ Knowledge, Attitudes, and Interest in VCA Treatment for Disfiguring Service-Related Injuries

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Background: Thousands of American service members have suffered catastrophic injuries to the head, face, and extremities resulting in functional limitations and significant disfigurement. The rise of vascularized composite allograft (VCA) procedures now allows for hand and face transplants, which can improve the functioning, mobility, and quality of life for these veterans, particularly those who have not responded well to available reconstructive procedures or prosthetics. Despite potentially life-enhancing outcomes, however, the awareness of and interest in this treatment option by VCA-eligible veterans is unknown. By examining this population’s receptivity to VCA, the study’s goal of identifying the assets and barriers to receiving a VCA will instruct more informed decision making about this treatment.

Methods: In collaboration with the Veterans Affairs Medical Center (VAMC) in Coatesville, PA, and the Department of Defense Joint Trauma Registry, over 1,100 medical records from 2010-2019 were reviewed for applicable ICD-9 codes. In-depth semi-structured interviews were conducted via telephone or video conference with up to 60 military veterans to examine current health status, treatments and therapies, impact of their injuries on daily life, and reactions to VCA, as the primary domains of inquiry. Interviews were audio-recorded for accuracy, deidentified, and transcribed for analysis. The existing domains and emergent themes formed the basis of a codebook, and MAXQDA software was used to facilitate qualitative coding of the data.

Results: Most participants interviewed to date, reported amputation of one or both hands. Although largely unfamiliar with the technical terminology of “Vascularized Composite Allograft transplantation,” most expressed familiarity with the procedure when described in more detail. While initial reactions were largely positive, many participants did not see this treatment as necessary for themselves. Multiple participants indicated greater receptivity if they were less adapted to their injury or did not have at least one functioning upper limb. Reported concerns included possible graft rejection, recovery time, medical fatigue, side effects of immunosuppression, and the effectiveness of the VCA procedure. Respondents identified more functional independence as the most critical and desired outcome of receiving a VCA graft in addition to navigating their day-to-day environments with fewer accommodations and adaptive equipment.

Conclusion: Participants viewed VCA as an interesting medical advancement and acknowledged its potential benefits but also expressed skepticism about its efficacy. These observations provide a knowledge base for researchers and practitioners engaged in growing the field of VCA. Further examination of the attitudes and experiences of the caregivers and healthcare providers of VCA-eligible patients would offer valuable perspectives in informing decision making about VCA.

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Combining Donor Derived Cell-Free DNA Fraction and Quantity To Detect Kidney Transplant Rejection Using Molecular Diagnoses


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Background: Donor-derived cell-free DNA (dd-cfDNA) fraction and quantity have both been shown to be associated with allograft rejection. The present study examined the relative predictive power of each of these variables to the combination of the two and developed an algorithm incorporating both variables to detect active rejection in renal allograft biopsies.

Methods: The first 426 sequential indication biopsy samples collected from the Trifecta study (ClinicalTrials.gov # NCT04239703) with microarray-derived gene expression and dd-cfDNA results were included. After exclusions to simulate intended clinical use, 367 samples were analyzed. Biopsies were assessed using the Molecular Microscope Diagnostic System (MMDxTM) and histology (Banff 2019). Logistic regression analysis examined whether combining dd-cfDNA fraction and quantity adds predictive value to either alone. The first 149 sequential samples were used to develop a two-threshold algorithm, and the next 218 to validate the algorithm.

Results: In regression, the combination of dd-cfDNA fraction and quantity was more powerful than either dd-cfDNA fraction or quantity alone, and validated a novel two-threshold algorithm incorporating both variables.

Conclusions: This prospective, biopsy-matched, multi-site dd-cfDNA study examined the relative predictive power of each of these variables to the combination of the two and developed an algorithm incorporating both variables to detect active rejection in renal allograft biopsies.

Clinical Validation of a Plasma Donor-Derived Cell-Free DNA Assay to Detect Allograft Rejection and Injury in Lung Transplant


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Background: Lung transplant patients are vulnerable to various forms of allograft injury, whether from acute rejection (AR) [encompassing acute cellular (ACR) and antibody-mediated rejection (AMR)], chronic lung allograft dysfunction (CLAD), or infection (INFXN). Previous research indicates that donor-derived cell-free DNA (dd-cfDNA) is a promising non-invasive biomarker for the detection of AR and allograft injury. The aim was to validate a clinical plasma dd-cfDNA assay for detection of AR and other allograft injury and to confirm and expand on dd-cfDNA and allograft injury associations observed in previous studies.

Methods: We measured dd-cfDNA fraction using a novel SNP-based assay in prospectively collected plasma samples paired with clinical-pathologic diagnoses. dd-cfDNA fraction was compared across clinical-pathologic cohorts: stable, ACR, AMR, isolated lymphocytic bronchiolitis, CLAD/neutrophilic-responsive allograft dysfunction (CLAD/NRAD), and INFXN. Performance characteristics were calculated for AR and combined allograft injury (AR+CLAD/NRAD+INFXN) versus the stable cohort.

Results: The study included 195 samples from 103 patients. Median dd-cfDNA fraction was significantly higher for ACR (1.43%, IQR:0.67-2.32%, p=5x10-5), AMR (2.50%, IQR:2.06-3.79%, p=2x10-5), INFXN (0.74%, IQR:0.46-1.38%, p=0.02) and CLAD/NRAD (1.60%, IQR:0.57-2.60%, p=1.4x10-6) versus the stable cohort (0.46%, IQR:0.21-0.78%) (Figure 1). Area under the receiver operator characteristic curve (AUROC) for AR versus stable was 0.91 (95% CI:0.83-0.98) (Figure 2). Using a ≥1% dd-cfDNA fraction threshold, sensitivity for AR was 99.1% (95% CI:76.2-100.0%), specificity 82.9% (95% CI:73.3-92.4%), positive predictive value (PPV) 51.9% (95% CI:37.5-66.3%), and negative predictive value (NPV) 97.3% (95% CI:94.3-100%). For combined allograft injury vs. stable AUROC was 0.76 (95% CI:0.66-0.85), sensitivity 59.9% (95% CI:46.0-73.9%), specificity 83.9% (95% CI:74.1-93.7%), PPV 43.6% (95% CI:27.6-59.6%) and NPV 91.0% (95% CI:87.9-94.0%).

Conclusion: These results indicate that dd-cfDNA can detect AR and other allograft injury. dd-cfDNA monitoring, accompanied by standard clinical assessments, represents a valuable precision tool to support lung transplant health.
Transplant of the Abdominal Rectus Fascia in Rodents, First Report of the Microsurgical Procedure, and Initial Results

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Introduction: After intestinal or multivisceral transplants, the proper management and closure of the abdominal wall becomes a challenge. The enterocutaneous fistulas, ostomies, skin scars secondary to multiple previous surgeries or frozen abdomen syndrome are some of the predisposing factors. Synthetic meshes usually produce complications associated with infections and fistulas when used in unfavorable environments, in addition to high costs. Some previous clinical studies have shown benefits applying wall reconstruction techniques including the variant of using a non-vascularized fascia of the abdominal rectus muscle, described by our team. The need to better understand immunological aspects of this procedure we have conceived the concept of performing a murine model.

Methods: The procedures were approved by the internal review board and ethics committee for the care and use of laboratory animals (CICUAL UF 2021-016, #PICT 2016-3677). Technical aspects were done reproducing the technique for humans, details and pitfalls are described as part of the results. Engraftment observations were made on days 7, 11, and 30 post-transplantation for each animal strain. At day 30, each recipient was sacrificed, serum and tissue samples were obtained (from the sheath, and the adjacent muscle tissue). Histological studies of the graft were performed.

Results: 6 transplants of the abdominal rectus fascia (TxARF) were performed. All donors were female Sprague Dawley rats, while the recipients were 3 Sprague Dawley (3 isogenic TxARF) and 3 Wistar females (allogeneic TxARF). The skin was separated, and the abdominal muscle wall was completely removed to then perform the dissection under a microscope (Fig. 1). TxARF was done utilizing a continuous suture kind Surget with 6-0 Prolene, after removing the ARF and muscle of the recipient (Fig. 2), the skin is closed over the fascia. Once the Tx was finish a strict clinical follow-up of each rat was carried out providing initial treatment with Tramadol and Ceftriazone; 30th day survival was 100%, 2 recipients developed seromas on days 5 and 11, both isogenic ARF. The visual observation of the grafts showed absence of tissue stiffness and the presence of macroscopic neovascularization (Fig. 3) None of the grafts presented visceral adhesions at the end of the observation period. On histological inspection, the grafts showed, no presence of leukocytes or apoptotic cells, the adjacent native muscle tissue did not present particularities.

Conclusion: This first report of the TxARF in rodents, proofs the feasibility of these experimental and translational model. Likewise, it shows similar results to the published in the clinical field, there was absence rejection and abdominal adhesions in the short term under a model without immunosuppression. Further studies will be done to evaluate the immunogenicity, the loss of strength and elasticity as well as the long term results of transplanting the ARF.
Patient Definitions of Transplant “Success” of Upper Extremity VCA

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Purpose: Little is known about how to measure “success” of upper extremity (UE) vascularized composite allotransplantation (VCA) given its relative novelty and low frequency. While providers define UE VCA “success” as survival, functional, and quality-of-life outcomes, patients’ definitions have been little examined. Our study assessed patients’ definitions of transplant “success.”

Methods: We conducted focus groups among people with acquired UE amputations and UE VCA candidates, participants, and recipients at two sites to assess transplant “success.” Focus group transcriptions were analyzed using thematic analysis. A post-focus group survey assessed demographics.

Results: We conducted 6 focus groups among 26 participants (90% participation rate), including people with acquired UE amputations (n=20), UE VCA candidates who did not pursue it (n=3), a waitlisted UE VCA participant (n=1), and UE VCA recipients (n=2). Most were male (62%), white (85%), and had a unilateral amputation (77%), with a mean age of 49. Transplant “success” was defined in 5 ways: 1) The surgical attachment of the donor limb without complication: “an arm has been transplanted onto your body without rejection”; 2) Restoring function and sensation in the transplanted limb to restore activities: “I can bring a glass to my lips and drink. I can open a door. Turn a doorknob. I can drive my car”; 3) Ensuring the transplant process (e.g., surgery, hand therapy, immunosuppression) ran smoothly: “you’re in rehab and moving forward and making the process work”; 4) Gaining greater functional and quality of life with UE VCA compared to no treatment or prosthetics: “How many different tasks can I do with my new hand versus residuals?”; and 5) Ensuring that functional and quality-of-life benefits outweighed the risks (e.g., recovery, side effects, financial): “The addition of the functional and quality benefits that UE VCA would offer to what I can do versus without UE VCA.”

Conclusions: Our findings suggest that people with UE amputations define transplant “success” based on desired treatment processes and outcomes, comparing UE VCA to alternatives. Patient-provider discussion about definitions of transplant “success” may help patients determine if UE VCA is the right treatment for them.

This study was funded by US Department of Defense research grants: Award #W81XWH-19-2-0033 (PI Dr. Elisa Gordon), Award #W81XWH-19-2-0034 (PI Dr. Macey Levan), Award# W81XWH-19-2-0035 (PI Dr. Gerald Brandacher), and Award# W81XWH-19-2-0036 (PI Dr. Scott Tintle).

Total Bilateral Arm Transplantation: Functional Recovery and Psychosocial Outcomes at One Year

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Introduction: Although arm loss causes severe disability and complications of body image, functional recovery after allotransplantation still presents major challenges.

Objective: A bilateral arm transplantation including reconstruction of the left shoulder was performed on January 13, 2021 in Lyon (France). Functional recovery and psychosocial outcomes are reported one year after the transplantation.

Materials and Methods: The recipient was a 48-year-old patient with bilateral amputation at proximal arm level after electric shock in January 1998, who underwent liver transplantation in 2002. The patient used mechanized prostheses with poor satisfaction. The surgical procedure consisted in a total arm transplantation on the left side with reconstruction of the gleno-humeral joint. The maintenance immunosuppressive therapy included tacrolimus, mycophenolate mofetil and prednisone. Rehabilitation therapy started on day one. It progressively included manual lymphatic drainage, passive motion of all joints in a total range except limitations for the shoulders during the first 6 weeks. Then, electrostimulation on denervated muscles was performed. After 6 weeks the protocol included hand therapy, psychomotor, physical activities, occupational therapy and sensory-motor simulation training approaches (motor imagery, virtual mirror therapy, virtual reality).

Results: Motor recovery was already appreciated 8 months after the transplantation. At one year, passive ranges of motion of upper limbs are subnormal. According to MRC scale, muscular strength at shoulder level is from 3 to 4/5 on the right side and from 1 to 2/5 on the left side; from 3 to 4/5 for elbow flexors and from 1 to 2/5 for elbow extensors on both sides; 3/5 for wrist flexors on the right side and 0/5 on the left side; 1 to 2/5 for wrist extensors on both sides; 3/5 for pronators and supinators on the right side and 1/5 on the left side. Slight contraction and movements of the extrinsic flexors and extensor muscles of the fingers have been evidenced on both sides, and the first prehension movements started on the right hand.

The Sessmers-Weinstein monofilament test for sensory threshold was 6.65 in the right palm and below the left elbow; deep pressure sensation is recovered in both hands. Functional Independence Measure is 96/126 and the DASH score 75.8. The patient is able to perform the same daily activities as with the prostheses before the transplantation. The patient was psychologically tested during the follow-up using a specific questionnaire for upper extremity allotransplantation and MADRS, Hamilton and Rosenberg tests. The results (Table 1) show the difficulties, the patient’s strong motivation and capacity to cope, and his satisfaction reached at the first year of follow-up.

Conclusions: The patient is very satisfied of his grafts and of his restored body image, which was his main expectation.

<table>
<thead>
<tr>
<th>M3</th>
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<tr>
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<td>20/60</td>
<td>24/60</td>
</tr>
<tr>
<td>Hamilton test</td>
<td>13/50</td>
<td>18/50</td>
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<tr>
<td>Rosenberg test</td>
<td>35/40</td>
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</table>

Table 1: The results of the tests at 3, 6 and 12 months. MADRS (Montgomery-Åsberg Depression Rating Scale) and Hamilton rating scale were used to evaluate depression severity, Rosenberg Self Esteem Scale is a self-esteem measure.
427.10

A New Era in Transplantation: Artificial Intelligence, Augmented Reality, Virtual Reality and Metaverse

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Introduction: Big data in healthcare and surgical sciences, combined with advances in computer technology and software, has brought healthcare and medical applications into the age of Artificial intelligence (AI), Virtual Reality (VR) and Augmented Reality (AR). These technologies have started to come to the fore even more with the metaverse era. The main purpose of this review is to discuss the advances and challenges of these methods in transplantation.

Method: In this systematic review study, we systematically searched for studies on MEDLINE, Scopus, Web of Science and Google Scholar. The concepts of AI, Machine Learning (ML), Deep Learning (DL), AR, VR and Metaverse which opened a new era in transplantation, were discussed and their application areas in transplantation in the literature were examined. Along with the benefits it will provide limitations and possible risky situations, disadvantages and especially the ethical dimension have been examined.

Results: AI is a scientific approach that uses theories and mathematical algorithms to give computer systems the ability to perform tasks that would normally require human intelligence. ML and DL algorithms in particular AI models will create a decision support system for the clinician at every stage related to the patient in transplantation. Some basic applications of AI in transplantation are seen in evaluations such as listing for transplantation, organ allocation algorithms, determining whether to accept the organ for a particular recipient, creating a clinical prediction and decision support system that will guide the physician, estimating mortality and morbidity in the waiting list, and post-transplant survival analysis. There are also examples of AI in image processing, organ allocation, donor and recipient matching, pathology, real-time immunosuppression, transplant oncology, and predictive analysis. VR and AR are areas of robotic surgery innovation in the coming years. VR is generally defined as an experience where a user stays physically in their real world while entering a virtual world using a computer or mobile device. AR is a technology that overlays digital information on real-world objects or places to enhance the user experience. Applications of AR in the field of transplantation include its use in the training of transplant surgeons, in promoting organ donations, in graft retrieval and allocation, and in the microscopic diagnosis of organ rejection, in the treatment of complications and post-transplant neoplasms.

Conclusion: In the digital age we live in, these methods should be used in the clinical decision-making process in the field of transplantation. In the coming years, clinical transplant professionals will increasingly use these models to support their decisions. With the use of these applications in transplantation, organ use can be optimized, complications can be predicted and pre-transplant management can be optimized, which can reduce the need for transplantation.

427.11

Assessment of Music Therapy on Psychological Stress And Immune Function in the Early Postoperative Period of Renal Allograft Recipients: A Prospective RCT

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Background: Patients who have recently received kidney transplantation are often accompanied with psychological stress such as depression and anxiety, as well as immunodeficiency owing to immunosuppressant application. Music therapy (MT) is more and more accepted in clinical practice not only to help patients relieve psychological stress, but influence their immunity. Therefore, we aimed to evaluate the effectiveness of MT on psychological stress and immune function in the early postoperative period of renal allograft recipients.

Methods: A one-month randomized controlled trial (RCT) has been carried out comparing MT to non-music therapy (NMT) for renal allograft recipients with regular medication after they finished surgery and stayed in hospital. 40 participants were randomly assigned to one of the two groups based on our inclusion and exclusion criteria. In MT group, Mozart sonata for two pianos K448 in D major (2nd movement) were given to patients for 30 minutes every night for ten consecutive days. Psychological scales (depression anxiety stress scale 21, World Health Organization Five-item Well-Being Index, Satisfaction with Life Scale) were given to patients three times (before, after and during the experiment); Peripheral immune cell subsets (T, B, NK cells) will be tested twice (before and after the experiment).

Results: Compared to NMT, he scores of negative psychological symptoms were decreased but the physical and mental health indices were increased in MT group. Absolute numbers of CD4+ T and B cells, as well as CD4/CD8 ratio, were increased in in MT group.

Conclusion: Our findings suggest that music therapy is helpful to relieve the psychological stress and enhance the immune function of renal allograft recipients with regular medication in the early postoperative period, which could provide clinical auxiliary rehabilitation therapy for transplant patients. This study was supported by grants from the National Natural Science Foundation of China (81700658) and the Hunan Provincial Natural Science Foundation-Outstanding Youth Foundation (2020JJ3088).
Using Artificial Intelligence to Classify the Status of Kidney Allograft in Routine Clinical Records

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Introduction: Electronic health records (EHRs) could be useful for research, but as they are not designed for this purpose, their use offers several practical challenges: regular access and selection of information that is generated at high volume and speed, expensive and time-consuming process of manual review and requirement of highly skilled personnel for identification and selection of relevant information with minimum error. Another major challenges in using these data is to identify the most relevant information, as the data in the EHRs are not collected for research purposes. Automated text classification using natural language processing (NLP) may help to overcome this challenge. The aim of this study is to develop an NLP algorithm to classify correctly the status (failure) of a kidney allograft in clinical records of kidney transplant recipients written in Spanish.

Methods: To train and evaluate the NLP tool, we used an annotated corpus of 61,382 clinical records from kidney transplant patients (n= 1,950) followed in Colombiana de Trasplantes from 2008 to 2021. A couple of trained clinicians who review every record classified graft loss events. We prepared the free text in the clinical records in several steps: data cleaning (removing punctuations, removing stop words, lower casing, tokenization and lemmatization), data transformation, data integration and data reduction. Using a machine learning model (random forests) we identified the most important words to classify graft loss in clinical texts. We used this model to classify the status of the graft in a testing dataset by using a method for validating the model (Bagging or Bootstrap Aggregation).

Results: A word cloud showed the most recurrent terms or concepts in the dataset. According to the mean decrease in Gini Score, the Spanish words that better identify graft loss in our clinical texts were: “pérdida”, “unidad”, “hemodiálisis” and “diálisis”. The random forest model correctly classified 94% of the events of graft loss (540/575).

Conclusion: A wealth of clinical histories remains locked behind clinical narratives in free-form text. NLP methods that automatically transform clinical text into structured data may help unlock the full potential of EHR data. We present promising preliminary results of an application of machine learning and NLP methods that classify automatically the status of kidney transplantation from unstructured text in routine clinical records, potentially helping to avoid the need of lengthy and expensive manual review for outcome classification in clinical research.
Optimizing Lung Function During Donor Management Through A Multidisciplinary Approach

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Introduction: In current healthcare, a multi-disciplinary approach is taken in critical care to ensure all specialties can offer their training and expertise in the care of every patient. In organ donation, and specifically donor management, having a team of Procurement Transplant Coordinators (PTCs) that is comprised similarly ensures that optimal results can be achieved through a varied knowledge base. Traditionally, this has been heavily weighted with Registered Nurses with critical care experience. We propose that including Registered Respiratory Therapists (RRTs) as PTCs can broaden the base of expertise of the team and maximize successful lung transplantation. Additionally, the incorporation of different modes and modalities of ventilation with a physiological approach to lung recruitment has successfully proven an increase in lung optimization.

Method: To fully understand the positive impact of RRTs in lung recruitment, we looked at the upward trend of the Horowitz index for Lung Function (P/F ratio) with a subject United States based Organ Procurement Organization and how it correlated with an increasing number of PTCs that are licensed and registered Respiratory Therapists. Four RRTs were onboarded to the donor management team during 2020 and 2021. Comparing the results from previous years, data showed a related increase in lung recruitment and optimization per year with RRTs working as PTCs.

Results: Evidence demonstrated a correlation of the increase in lung procurement and transplantation numbers mirroring an increase in RRTs in the role of PTCs. Improvements to P/F ratios were compared at the beginning of the case to the final P/F ratio prior to OR. From January 1, 2018-December 31, 2019 there were 89 donors who were brought to the operating room for lung procurement with the intent of transplantation. The median and mean improvement to P/F ratios were +0.83 and +0.83, respectively. From January 1, 2020-December 31, 2021 there were 75 donors who were brought to the operating room for lung procurement with the intent of transplantation. The median and mean improvement to P/F ratios were +1.04 and +1.32, respectively. This proved a 25.3% increase for the median PF ratio and a 59% increase to the mean PF ratio.

Conclusion: Our research supports that PTCs who are licensed and experienced Respiratory Therapists being proficient in lung physiology, recruitment, and ventilation strategies contribute to an increase in lung optimization. With having specific organ expertise, RRTs have proven to be a vital asset while sharing knowledge with the entire multi-disciplinary team.

P1.02

Training and Social Awareness Targeted for Allied Health Professionals for Increasing Organ Donation in the European Union and Neighboring Countries: EUDONORGAN

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Introduction: EUDONORGAN is a service contract awarded by European Commission on initiative of the European Parliament aiming to provide training and increase social awareness in the European Union (EU) and neighboring countries to enhance positive attitude towards organ and tissue donation, ultimately help improving donation rates.

Methods: Spain as leader, Croatia, Italy & Slovenia joined the project and took responsibilities in work packages: a) WP1-Training b) WP2- Social Awareness; c) WP3- Dissemination and d) WP4- Evaluation. Selection criteria for training beneficiaries (healthcare professionals and other key players) were provided to Competent Authorities of Member States (MS) and patient associations to propose candidates. In WP1, the training program employed a blended methodology. The beneficiaries included healthcare professionals (HPs) and other key players (OKPs) from the EU and NCs. The e-learning offered one route for HPs and another for OKPs, each one of them involved eight short videos explaining tissue and cell donation. The face to face was practical and promoted best practice exchange. A survey on attitude towards donation was carried out among participants before and after. In WP2, donation data was collected from EU and NCs for the organisation of six tailored awareness events in 2018-2019.

Results: In WP1, 101 participants from 28 countries completed the training: 79 HPs and 22 OKPs. The e-learning was evaluated with 4.45 (from 1-poor to 5-excellent), registering 25.22% of knowledge improvement among healthcare professionals and 29.47% among other key players. The face-to-face session was evaluated with 4.44 (from 1 to 5), 96 participants attended all sessions and were certified. In WP2, 6 Member States to organize awareness raising events in Warsaw, Budapest, Brussel, Stockholm, Lisbon, and Athens. The events involved more than 500 participants from different countries. Nowadays, project materials are being translated to Chinese, Greek and other languages to continue with the dissemination of the project.

Conclusion: EUDONORGAN is an innovative cross-sectorial project that aims at improving donation across the European Union and neighbouring countries.
Knowledge Exchange Program to Increase the Organ Donation Rates in Saudi Arabia

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1Donation and Transplantation Institute (DTI Foundation), Barcelona, Spain; 2Saudi Center for Organ Transplantation, SCOT, KSA, Saudi Arabia.

Introduction: World Health Organization is advocating for the development of self-sufficiency in donation and transplantation (D&T) worldwide. Since 2017, the Ministry of Health of the Kingdom of Saudi Arabia (KSA) launched a program coordinated by DTI Foundation (DTI) with the support of the Saudi Center for Organ Transplantation (SCOT) aiming to improve the deceased donation rates by implementing educational programs and quality management systems. The present study summarizes the effect of the implementation of a quality indicators pilot program and training programs in the KSA’s critical pathway for organ donation.

Methods: The DTI-SCOT collaboration has included: a) diagnosis study to achieve a comprehensive vision of donation system (2017); b) implementation of a pilot program to maximize the donor referral in 6 centers; c) monthly follow-up to analyze the data collected leaded by international experts; d) external audits and e) implementation of four intermediate TPM online training at national level (2020-21).

Results: The collaboration allowed to identify the organizational, structural, and educational needs. At the pilot program hospitals, the donation alerts increased from 100 to 298 during the first year of the project (250 of these were potential, 101 eligible and 26 were actual donors). This represented an increase in potential donor detection and referral and a final 44% increase in the donation rate. So far, more than 250 ICU professionals from near 200% increase in potential donor detection and referral and a final 44% increase in the donation rate. So far, more than 250 ICU professionals from 100 to 298 during the first year of the project (250 of these were potential, 101 eligible and 26 were actual donors). This represented an increase in potential donor detection and referral and a final 44% increase in the donation rate.

Conclusions: The collaboration with DTI made possible to establish new donor detection and audit methodologies. In-hospital protocols were reviewed and redefined, specifically those related to brain death diagnosis and donor maintenance. As seen in Figure 1, during 2020, 113 deceased donors were reported. Therefore, 342 deceased organ transplantations were performed.

<table>
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<tr>
<th>Year</th>
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</table>

Development of an Intelligent Digital Biosurveillance Platform

Barbara De Aquilina Pozza1, Vanessa Silva e Silva2, Karina Dal Sasso Mendes3, Patricia Treviso4, Tadeu Thomé5, Valter Duro Garcia6, Liliana Camera Pierrotti7, Alvaro Machado Dias8, Janine Schirmer1.
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This is a study on the development of an intelligent digital platform for Brazil. The platform is capable of recording structured and unstructured data in Web and Mobile environments, of sending the automatically compiled data to remote servers, of generating computational panels of analytical results (dashboards), capable of supporting the production of insights. The platform (https://biovigilancia.org/home) built for the National Biovigilance System aims to:

1. (1) Allow the continued recording of new adverse events, in a 100% user-friendly manner. (2) Allow surveys to be carried out with different stakeholders: donors/recipient, hospital managers, health professionals and researchers/teachers. (3) Generate graphs for intuitive visualization of the indicators collected in the surveys, through a results dashboard. (4) Ensure a system of restrictive access so that information of general interest is public, while those with more sensitive characteristics remain accessible only to representatives of the institutions involved in the project.

The platform is divided into three parts (Figure 1):

- Situational research: recurrent mapping of adverse events involving human cells, tissues and organs for transplantation.
- Report an adverse event: register here any adverse events related to human transplants and help Brazilian Biovigilance fulfill its role.
- Restricted functions: this area is intended for researchers and health managers directly involved in the project, with login and password access.

Adverse event reporting is based on the structure of the Notify Library (https://www.notifylibrary.org/) and is designed to allow for broad inclusion and exclusion of variables. Its basic structure separates adverse events as donor-related and recipient-related.

The main restricted functions of the platform are: consultations on sensitive research or not yet publicly disclosed and consultations on the results dashboard involving strategic actions that in some way may be negatively affected by the wide publicity.

The operations of this section came from the implementation of a multi-user authentication system, which allows us to approve specific registrations, blocking subjects without the necessary permissions, as well as cyber attacks.

The National Biovigilance System Platform dashboard is based on a data visualization framework called Shiny. It has graphics of high visual appeal and great informational power.

The idea is that the dashboard is continuously fed with collected and reported data, so that the visualizations are always current. We are currently developing artificial intelligence on the platform so that we can predict the next adverse events and thus contribute to improving safety in the therapeutic use of organs, tissues and cells.

Gender and Transplantation. the Impact of the Social Role of Gender and Its Implications in the Process of Health-Illness and Care

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Introduction: It is well known that an illness, in most cases, entails an interruption in the process of health-illness-attention and care of people (PSEAC). However, research from a gender perspective has shown several differences in the ways men and women experience illness and adhere to treatment.

Objective: From our experience as social workers, we intend to know how gender roles impact on the process of health, attention and care of people with a chronic pathology, and how they affect daily life as a whole. In order to carry out the study, an interview sample of patients in the pre-transplant stage were conducted by the Social Workers, who work in the Renal and Liver Transplant Services of the Hospital General de Agudos of the City of Buenos Aires. Period: June 2021 to February 2022.

Methodology: Through a gender perspective, a qualitative study was conducted using the ethnographic method (Guber, 2001), the discourses collected in semi-structured interviews with patients attended by these teams were categorized, interpreted and analyzed.

Results: From the analysis of the interviews, it is observed that, as a result of their illness, men see their work, recreational and social tasks affected, while women, conversely, have a greater impact on their domestic, care and parenting activities. This reflects the organization of care within households, which depends mainly on the non-remunerated work carried out, to a greater extent, by women. Thus, chronic renal and hepatic pathologies not only affect women, but also disrupt the dynamics and organization of care within a family group, as well as the daily life of women and their family members, impacting the process of their treatment, recovery and health care.

Conclusions: From our understanding, the gender perspective, which provides us with a new perspective on how to address health problems, offers health teams the opportunity to create spaces capable of strengthening accessibility to the target population by constructing intervention strategies in accordance with the particularities and needs of the patients treated in transplant care services.
P1.06

Exploration of the Influencing Factors of the Self-management in Renal Transplant Recipients Based on the Health Promotion Model

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Background: Self-management is the key point to maintain the graft kidney function and the survival of renal transplant recipients. However, the level of self-management is not adequate and the factors influencing self-management in renal transplant recipients were not studied sufficiently.

Objective: This study was to explore the influencing factors of the self-management in renal transplant recipients based on the Health Promotion Model.

Methods: Data was collected from 270 kidney transplant recipients who were regularly followed up at the outpatient clinics of three tertiary hospitals by convenience sampling method. The survey tools used included General Information Questionnaire, Kidney Transplant Recipient Self-management Support Scale, Self-efficacy for Managing Chronic Disease 6-Item Scale, Kidney Transplant Recipient Self-management Scale, and Hospital Anxiety and Depression Scales. SAS 9.40 and Amos 24.0 were used for statistical analysis of the data.

Results: The self-management scores of renal transplant recipients were: Problem solving = 35.00 (30.00, 40.00), Partnership was 14.00 (12.00, 16.00), Self-care was 45.00(40.00, 49.00), and the score indexes were 86.54%, 87.50% and 87.50% respectively. The results of structural equation model showed that the final model had significant consistency with the data. Economic burden, work status, habitual residence, education level, depression, anxiety, self-efficacy and self-management support accounted for 42% of the variance on self-management. The order of the total effect of each factor on self-management from high to low is: self-management support (β = 0.056), anxiety (β = 0.243), education level (β = 0.191), self-efficacy (β = 0.165), habitual residence (β = 0.112), economic burden (β = 0.069), depression (β = 0.017), and work status (β = 0.013).

Conclusion: We can explain the influencing factors of self-management in renal transplant recipients using the Health Promotion Model. The overall level of self-management in renal transplantation recipients is high, but there are still differences among different groups of characteristics. The self-management in renal transplant recipients was mainly affected by self-management support and anxiety. The transplant professionals should pay attention to these influencing factors when making interventions to improve the level of self-management in renal transplant recipients. Keywords: health promotion model; kidney transplantation; self-management; self-management support.

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P1.07

A New Intervention to Increase Medication Adherence in Kidney Transplant Recipients: Investigation of Effect of SystemCHANGE Intervention

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Introduction: In all organ transplant recipients, immunosuppressive drugs are important in terms of the prevention of rejection, transplanted organ and patient survival. Non-adherence with immunosuppressive drugs is an important problem affecting patient outcomes in kidney transplant recipients. Medication adherence intervention studies are not theory based, intervention effect sizes are low, and studies lack methodologic rigor. The primary aim of the study is to evaluate the effect of the SystemCHANGE™ intervention applied in kidney transplant recipients on medication adherence. The secondary aim is to examine the effects of the SystemCHANGE™ intervention applied in kidney transplant recipients on the health outcomes (infection, rejection, graft loss, death, blood urea nitrogen and creatinine level) and quality of life.

Method: The study used a randomized controlled single-blind study design. Electronic medication monitoring was used for three months to screen for medication nonadherence. Medication adherence was measured by the Medication Event Monitoring System SmartCap® (MEMSCap™). Participants with a high level of medication adherence (> = 85) were excluded from the study while those with medication nonadherence (< = 85) were randomized into the study. The intervention group received the 6-month SystemCHANGE™ intervention and the attention control group received the 6-month patient education intervention. The follow-up phase continues six months after the intervention when no intervention is delivered. Infection, rejection, graft loss, death, blood urea nitrogen and creatinine level of the participants were evaluated. Quality of life level was evaluated by SF-36.

Results: The 6-month intervention phase of the study has been completed and the 6-month follow-up period is currently being delivered. Results of the study will be presented at the congress.

Conclusion: This study is the second in the international literature to evaluate the effect of a new intervention-SystemCHANGE™, on medication adherence in kidney transplant recipients and the first to evaluate in Turkish kidney transplant recipients. This research is supported by TUBITAK 1001 - Support Program for Scientific and Technological Research Projects with project number 218S720. We thank TUBITAK for their support.
IL-33/ST2 Signaling Pathway: Preliminary Study to Assess Its Role in Chronic Rejection After Liver Transplant

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Introduction: The improvements in the immunosuppression therapies have reduced the prevalence of chronic rejection (CR) of liver allografts, however CR still represents an important cause of graft loss requiring re-transplantation. The biological mechanisms underlying this process remained not completely understood. IL-33 and its receptor (ST2) play important roles in the immune regulatory pathways including tolerance and cirrhosis development and virus infection. To the best of our knowledge, no reports are available describing its role after liver transplant (LT).

Objective: Studying the IL-33/ST2 axis in CR after liver transplant in humans.

Methodology: Liver tissue samples obtained at the time of liver transplantation from donors (Control Group, n=9) and liver tissue obtained from LT (n=12) patients were included in the study. Samples were retrospectively pooled into three groups: NR (No Rejection, normal without any histopathological signs of rejection, n=4), NR-LD (without any histopathological signs of rejection, but presenting liver disease of different causes (i.e., toxic damage, n=5) and CR (chronic rejection, with positive histopathological findings, n=3). Correlation analysis was made using the Kruskal–Wallis with Dunn’s post-test. Correlations were evaluated with the Spearman rank correlation test. The present protocol was approved by the Institutional Review Board of HUFF (DDI [1490] 2419).

Results: Hepatic levels of IL33 were not statistically different among groups. Nevertheless, the expression of ST2 was significantly higher in liver samples obtained from patients in CR and NR-LD groups (p< 0.05) (Figure 1). Then, we investigated whether ST2 levels were associated with hepatocellular and cholestatic damage, finding that ST2 correlated positively with TGFβ, ALT and ALP levels (p<0.05). Considering that Hepatic Stellate Cells (HSC) are the main source of ECM and collagen and its activation is dependent on IL-33/ST2 signaling, the activation marker α-SMA and the principal profibrogenic cytokine, TGF-β, were evaluated by qPCR in liver tissue. Levels of α-SMA, and TGF-β were increased in the CR group compared with the controls and the NR group, but these differences were not statistically significant. Moreover, the expression of α-SMA positively correlated with METAVIR score in LT patients (p<0.05).

Conclusion: Our preliminary data indicate that the IL-33/ST2 pathway is modulated in liver allograft in response to damage. Further studies in larger series need to be performed to obtain more insights into the biological function of this axis.

Figure 1: Patients with CR and liver injury presented higher levels of ST2 in liver tissue. Expression of ST2 was evaluated by qPCR in the Control (n = 9), NR-norma (n=4), NR-LD (n=5) and the CR (n = 3) groups. The values are the mean ± SEM. Comparison was performed by Kruskal–Wallis test along with Dunn’s post-hoc test.

Save the Environment: Liver Transplantation Restores A Circulating Environment That Supports Healthy Platelet Aggregation Within Two Hours of Reperfusion

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Introduction: Thrombocytopenia in patients with cirrhosis is common and likely multifactorial secondary to splenic sequestration, decreased thrombopoietin production, shear stress of portal hypertension, and toxic suppression of megakaryopoiesis. However, there is no clear association of absolute platelet count with risk of hemorrhage. Rather, platelet dysfunction, in the pro-inflammatory vasodilatory state of chronic liver disease, may be of greater importance. There is evidence that the circulating environment of severe tissue injury and shock impairs platelet aggregation in trauma patients. Using this model as our template, we hypothesized that healthy platelets treated with serum from cirrhotic patients pre-transplant would have impaired aggregation compared to those treated with serum post-portal reperfusion.

Methods: Serum was collected from liver transplant recipients prior to reperfusion, and two hours following portal reperfusion as part of the Mild Hypothermia and Acute Kidney Injury in Liver Transplantation trial (NCT03534141). Platelets (from male and female healthy platelet donors) were isolated by centrifugation, pellet, and mixed with each of the following sera (6 of each group): buffer, autologous, gender matched healthy (heterologous), gender matched pre-transplant, and gender matched post-portal reperfusion (12% v/v) for 20min (Fig1A). Baseline aggregation was measured for 10min via a multi-mode impedance aggregometer, then stimulated with a thrombin analog and measured for 15min. Aggregometry responses were quantified by the area under the impedance aggregation curve (AUC), normalized to autologous treated platelets. Statistical analysis was performed using one way ANOVA, with Tukey’s Honest Significant Difference testing post-hoc for pairwise comparisons.

Results: Healthy platelet aggregation was markedly impaired upon treatment with pre-transplant serum, but was restored when treated with serum from the same cohort of patients two hours post-portal reperfusion (to levels similar to treatment with healthy sera, Fig1B). Healthy platelet aggregation upon treatment with post-portal reperfusion serum was significantly higher than with pre-transplant serum treatment (median relative AUC 1.4x vs -0.1x, p<0.05; Fig2).

Conclusion: Healthy platelets treated with serum from cirrhotic patients immediately prior to liver transplant have impaired aggregation, while treatment with serum from the same patients two hours post-portal reperfusion restores aggregation. This suggests the circulating environment of cirrhosis may induce platelet dysfunction through soluble inhibitors, and that liver transplantation and the healthy plasma administration accompanying the reperfusion phase, may induce swift recovery of platelet aggregation capacity. Future investigations should focus on implications of this including that platelet transfusion may not achieve hemostasis until post portal-reperfusion.
Dynamic Kidney Rejection Risk Prediction Using Serial Donor Derived Cell Free DNA.

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Background: Donor-derived cell free DNA (ddcfDNA) has evolved as a non-invasive biomarker for monitoring kidney transplant patients for rejection. Trends in ddcfDNA over time may help predict important outcomes for the allograft. We examined samples from subjects enrolled in the CTOT08 clinical trial (NCT01289717) to determine the ability of joint modeling to dynamically predict rejection episodes (clinical and subclinical) in kidney transplant recipients.

Methods: Serial blood samples collected in the first two years post-transplant were analyzed for ddcfDNA using the TRAC test (Eurofins – Viracor, Lees Summit, MO). We used the joint modeling method to model the trend of serial ddcfDNA scores to predict the 2-year rejection-free probability. We pre-defined 4 time points post-transplant and dynamically plotted two illustrative patient’s 2-year event-free probability via the joint modeling method.

Results: The figures depicting the predicted event-free probability are presented as below. The two patients have very similar predicted 2-year event-free probability based on their serial TRAC score up to 0.17-years post transplant. Moving forward in time, the predicted probability starts to diverge for these two patients. One patient has stable ddcfDNA scores below 0.5% up to year 0.75. The patient’s predicted 2-year event-free probability increases over time. At 0.5-year post transplant, the predicted event-free probability is 0.621 [0.503, 0.737]. While for the other patient, their ddcfDNA score is relatively high and continues to increase. The second patient has a lower 2-year event-free probability. At 0.5-year post transplant, the predicted event-free probability is 0.548 [0.360, 0.702]. The patient went on to have a rejection episode at 0.86 months post-transplant.

Discussion: Plasma ddcfDNA is evolving as both a diagnostic and a prognostic biomarker in the management of kidney transplant recipients. Using joint modeling, we were able to develop a dynamic risk prediction model for future rejection episodes in patients. Future applications include further validation and eventually defined interventions such as immunosuppression titration to reduce the risk of future rejection episodes.
Polymorphisms Rs1800469, Rs1800471 of the Tgfb1 Gene Detected in Patients with Chronic Heart Failure who Waiting Cardiac Transplantation.

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Introduction: Chronic cardiovascular disease (CVD) is the most common cause of death in many countries around the world. The genetic mechanisms underlying the pathogenesis of CVD are not fully understood. It has been shown that transforming growth factor β1 regulates the production of the intracellular matrix, inhibits the proliferation of vascular smooth muscle cells, disrupts the division and migration of endothelial cells, which can contribute to the development of coronary heart disease. The aim was to estimate the impact of three types of TGFβ1 gene polymorphism (rs1800469, rs1800470, rs1800471) in patients with terminal heart failure who waiting cardiac transplantation.

Materials and Methods: The study included 110 patients (99 men; 44±14 years) with heart failure caused by dilated (57 cases) or ischemic (53 cases) cardiomyopathy. The comparison group was healthy blood donors (n=64). Single nucleotide polymorphism (SNP) (rs1800469, rs1800470 and rs1800471) of TGFβ1 gene was studied by TaqMan SNP genotyping assay.

Results: The pts. had next frequencies of the investigated alleles: rs1800469 - 20% AA homozygotes, 38% AG heterozygotes, and 42% GG homozygotes; rs1800470 – 83% AA, 13% AG, 4% GG; rs1800471 – 3% GG, 13% GC, 84% CC. The SNPs frequencies in the donors had next profile: rs1800469 - 15% AA, 34% AG and 51% GG; rs1800470 - 85% AA, 15% AG and 0% GG, and rs1800471 – 0% GG, 6% GC, 94% CC. There was deviation from Hardy-Weinberg equilibrium in distribution of SNPs rs1800469 and rs1800470 in cardiac pts. In healthy donors all the investigated SNPs were in Hardy-Weinberg equilibrium. Carriers of the genotype CC (p = 0.037, OR = 0.23, 95% CI: 0.054-1.031) and more often the allele G of rs1800471 (p = 0.037, OR = 4.2, 95% CI: 0.970-18.55) were found in patients less often than in healthy individuals. In patients with ischemic heart disease, the genotype GG was less common (p = 0.035, OR = 2.68, 95% CI: 1.061-6.793) and more often the allele A of rs1800469 (p = 0.035, OR = 0.37 95% CI: 0.148-0.942) than in patients with dilated cardiomyopathy.

Conclusion: The frequency of rs1800471 TGFβ1 differs between patients and healthy individuals. Allele A rs1800469 TGFβ1 is associated with ischemic heart disease in potential heart transplant candidates.
Influence of Adding Calcium Channel Blocker Verapamil During Perfusion for Functioning Transplanted Kidney Within 36 Months After Transplantation (Mid Term Results)

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Optimal method of preservation is the one of most important problems in organ transplantation. Flushout blood and metabolites, quick decreasing temperature of harvested organ, saving organ vitality are important points for good results of transplantation. In our research we tried to answer how much calcium channel blocker, Verapamil decreases kidney vessel resistance during harvesting and preservation how calcium channel blocker influence for graft after 12, 24 and 36 months after transplantation. Many authors imply that calcium plays central role in the pathogenesis of preservation injury and loss of organ viability. We analyzed 38 kidney cadaver-donors and 76 transplanted patients. Before starting gravity perfusion we injected intraarterial Verapamil solution directly to the one of the renal artery. We measured transplanted patients. Before starting gravity perfusion we injected intraarterial Verapamil solution directly to the one of the renal artery. We measured on the back table renal flow of perfusion solution (Eurocollins) in one minute of each kidney. Patients after kidney transplantation were divided in two groups, first group of patients using intraarterial Verapamil and second group without it. We observed in group of recipients with graft after injecting Verapamil improved graft function after transplantation by measurement diuresis, level of creatinine and urea in 12, 24 and 36 months.

A Survey of Transplant Recipient Attitudes Regarding Contraception and Pregnancy

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Background: While transplant professional society recommendations regarding contraception and pregnancy after solid organ transplantation (SOT) exist, counseling varies and some physicians discourage pregnancy. Patient preferences and attitudes about these issues are largely unknown.

Methods: Informed by the literature, we developed a survey instrument that was piloted among SOT recipients and conducted cognitive interviews to ensure item clarity. Items included multiple choice questions regarding contraceptive options and Likert scales about pregnancy concerns (i.e., 1-not at all concerned, to 5-extremely concerned) and attitudes (i.e., 1-does not describe their feelings, to 5-clearly describes their feelings). The survey was administered using Qualtrics in the posttransplant clinics at U Penn and Columbia University. All female SOT recipients aged <50 yrs were eligible. We used descriptive and inferential statistics to characterize participant views.

Results: 243 women completed the survey. Mean age was 37.5 yrs (SD 8.1 yrs); 46.1% were White, 29.2% were Black and 16.5% were Latino. Most participants had received a kidney transplant (66.7%), but 7% had a kidney-pancreas, 14.4% a liver, 13.2% a heart and 7% a lung transplant; 6.5% were multi-organ recipients. Of the 45.3% who reported currently using contraception, condoms (41.8%), intrauterine devices (26.4%), withdrawal (12.2%) and the combination pill (10%) were most common; side effects and contraceptive choices were the main reasons for contraception method selection. Only 42% of participants recalled signing the mycophenolate REMS. Prior pregnancy was common (60.1%), and 38.3% were considering pregnancy in the future. Acute rejection (mean 2.55, SD=2.45) or loss of transplant function (mean 2.58, SD=1.45) were less salient among most respondents compared to other potential pregnancy concerns. While concerns about maternal (mean 2.90, SD=1.42) or fetal (mean 2.93, SD=1.49) complications were moderate overall, they were lowest among liver recipients (mean 2.33, SD=1.31; mean 2.48, SD=1.59, respectively). Generally, respondents did not support the sentiment that transplant recipients should not become pregnant (mean 1.90, SD=1.15) nor that a limited life expectancy was a justification for avoiding pregnancy (mean 1.91, SD=1.09); with liver and kidney recipients were most strongly opposed. Among all participants, strong support was expressed for decisions around pregnancy being made jointly by the patient and the transplant team together (mean 4.17, SD=1.15).

Conclusions: Contraceptive use was not universal, and some of the most common methods have high failure rates. Side effects and familiarity drive contraceptive choice. Many SOT recipients are interested in posttransplant pregnancy and wish to make these decisions together with the transplant team. There were differences in views among respondents by transplant type, highlighting the need for individualized conversations.
P2.07

**ASXL1 May Promote the Differentiation and Function of TH17 Cells**

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**Introduction:** Kidney transplantation is the most effective method for the treatment of end-stage renal disease. However, immune rejection always restricts the survival rate of the graft. TH17 cells play an important role in renal transplantation rejection while the mechanism regulating TH17 cell differentiation and function is not fully understood. Asxl1 is an epigenetic regulatory factor frequently mutated in myeloid malignancies, but the role of Asxl1 in immune rejection or T cell development and differentiation has not been reported.

**Method:** Lymph nodes were isolated from wild-type mice (CD4Cre-Asxl1F/F, WT) and CD4+ T cell conditional Asxl1 knockout mice (CD4Cre+Asxl1F/F, KO), and CD4+CD25-CD44-CD62L+ naive T lymphocytes were sorted by the method of flow cytometry. The sorted cells mentioned above were stimulated with IL-1β (10ng/ml), IL-23 (50ng/ml), IL-6 (50ng/ml), TGF-β (5ng/ml), anti-IL-6 (10 μg/ml) and anti-IFN-γ (10 μg/ml) according to the cell density of 1×10⁵/well for 72 h, and then Monensin (2 μmol/L), Brefeldin A (5 μg/ml), Ionomycin (0.5 μg/ml) and PDBU (1 μmol/L) were added for further stimulation for 4 h at 37°C and 5% CO2. The stimulated cells were collected and the number and proportion of CD4+IL-17+ cells were analyzed by flow cytometry. The differentiation of TH1, TH2 and Treg cells were induced from WT mice by similar methods in vitro, and the expression of Asxl1 in different cell subsets were detected by Real-Time PCR at mRNA level.

**Results:** Compared with the WT mice, the number and proportion of TH17 cells in KO mice were significantly decreased. The mRNA expression level of Asxl1 in TH17 cell subsets from WT mice was the highest.

**Conclusion:** The results suggest that Asxl1 may promote the differentiation and function of TH17 cells as a positive factor. Asxl1 may become a new immune rejection target to regulate the number or function of TH17 cells, which has potential clinical significance in the intervention and prevention of rejection after kidney transplantation.

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P2.08

**Evaluation and Maintenance of Donor Liver Quality in Rats From Donated After Cardiac Death by Hypothermic Oxygenated Machine Perfusion and Cold Storage**

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**Objective:** To investigate the effects of hypothermic oxygenated machine perfusion (HOPE) and cold storage (CS) on liver quality in rats from donated after cardiac death after liver transplantation, it would to provide effective ideas for clinical evaluation and repair of DCD liver.

**Methods:** Twenty male SD rats were randomly divided into three groups (n=5): normal group is untreated group, cold storage group (CS group) and hypothermic oxygenated machine perfusion group (HOPE group). The DCD model was established by cardiac arrest caused by asphyxia. The rat liver was induced 30min of in-situ warm ischemia and then to be placed in 4°C UW solution for 4h (CS group), and the liver was placed in 4°C UW solution for 3h and hypothermic oxygenated machine perfusion for 1h, it was the HOPE group. The liver of DCD of each group received orthotopic liver transplantation. Blood and tissue samples were collected 30min, 1h, 6h, 12h and 7 days after the operation, respectively. The levels of ALT, AST and LDH in serum were detected by automatic biochemical analyzer, the levels of IL-1β and TNF-A in serum were detected by ELISA, and the morphological changes of liver were observed by HE staining, and the postoperative survival rate was evaluated.

**Results:** The levels of ALT, AST, LDH, IL-1β and TNF-a in CS group were higher than HOPE group, and the differences were statistically significant (p<0.05). The peak values of ALT appeared at 6h after reperfusion, with an average of 4000±385U/L. The peak values of AST and LDH both appeared at 1h after reperfusion. The mean values were 1700±743U/L and 75,000±2100U/L, respectively. One hour after transplantation, HE section of liver showed obvious hepatic cell edema, closed hepatic portal area, red blood cell aggregation in hepatic sinusoids, punctured necrosis of some tissues, structural destruction, and a large number of inflammatory cells infiltration. In the HOPE group, the hepatic sinus was enlarged, the structure of the portal area was relatively intact, and the infiltration of red blood cells and inflammatory cells was significantly less than that in the cold preservation group. The 7-day survival rate of normal group, CS group and HOPE group was 100% (5/5), 20% (1/5) and 40% (2/5), respectively. The main cause of postoperative death was pulmonary infarction (<24h).

**Conclusion:** HOPE has obvious advantages over CS in repairing DCD donor liver. HOPE can improve the microcirculation of DCD donor liver and reduce the incidence of pulmonary infarction, thus promoting the repair of DCD liver function.

Key words: hypothermic oxygenated machine perfusion, cold storage, donated after cardiac death, liver.

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Distinct Global DNA Methylation and NF-κB Expression Profile of Preimplantation Biopsies From Ideal and Non-ideal Kidneys

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Background: Epigenetic mechanisms may differently affect the ideal and non-ideal kidneys and their inflammatory gene expression profile and may contribute to poor clinical outcomes.

Objective: To identify the Global DNA methylation was evaluated, as well as the expression profiles of the DNA methyltransferases (DNMTs) and nuclear factor kappa B (NF-κB) in preimplantation kidney biopsies from ideal and non-ideal kidneys (extended criteria donor-ECD and with KDPI>85%).

Methods: Global DNA methylation was estimated by LINE-1 repeated elements methylation using bisulfite pyrosequencing, DNMTs expression was assessed by q-PCR and NF-κB protein expression by immunofluorescence.

Results: ECD kidneys displayed increased methylation levels in LINE-1, and DNMT1 and DNMT3B expression were upregulated when comparing ECD to standard criteria donor kidneys. Similarly, kidneys with KDPI > 85% exhibited increased LINE-1 hypermethylation and DNMT1 upregulation vs. kidneys with a KDPI ≤ 85%, NF-κB protein expression levels were greatly increased in both types of non-ideal kidneys compared to ideal donor kidneys. Moreover, hypermethylation of LINE-1 was associated with cold ischemia time > 20h and ECD kidney classification.

Conclusions: This study shows that global DNA hypermethylation and high expression of NF-κB occurred in both types of non-ideal kidneys and were associated with prolonged cold ischemia time. Global DNA methylation can be a useful tool to assess suboptimal kidneys and hence, could be used to increase the use of these kidneys to expand the donor pool.

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Single-Cell Transcriptomic Analysis of Peripheral Blood Reveals the Disparate Subsets of Innate Immune Cells in Kidney Transplant Recipient With BK Virus Infection

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Purpose: BK virus (BKV) infection is a common problem in kidney transplant recipients receiving immunosuppressive therapy, resulting in a serious complications including BKV-associated nephropathy and subsequent allograft loss. The purpose of this study was to characterize the disparate blood subsets in BKV infection/nephropathy at the single-cell transcriptional level.

Methods: We isolated peripheral blood mononuclear cells from three kidney transplant recipients with stable status, BK viremia and BK nephropathy. Single-cell libraries were generated using the 10x Genomics Chromium Platform. We analyzed multiplexing data in Cell-Ranger Pipeline and used R and “Seurat” packages for downstream analysis.

Results: A total of 14,031 cells were analyzed, including 5473 cells from stable patients, 3976 cells from patients with BK viremia, and 4582 cells from patients with BK nephropathy obtained from Illumina HiSeq X. We characterized 17 distinct clusters representing different cell types. Of these, 13 clusters had differentially expressed transcripts for each sample, and the most differentially expressed markers were S100A8, CCR7, LT, GZM, GZMK, GZMH, MT-CO1, LINC02446, IGC, AIF1, HLA-DRA, STMN1. Stable patient had more mRNA upregulated in B cells compared to patients with BK virus infection. In BK viremia, NK cells and monocytes were downregulated, whereas in BK nephropathy, mRNA expression was high in gamma delta T cells.

Conclusions: Our study revealed that BK virus infection/nephropathy induce unique characteristics in lymphocytes, which could be confirmed through single-cell RNA analysis. Further studies are needed to characterize the innate immune cells involved in the progression of BK nephropathy.
P2.13

Immunosuppression Monotherapy Does Not Protect Donor Leukocytes From Depletion Post MHC-Mismatched Kidney Transplantation in Mice

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Background: The retention of donor tissue-resident leukocytes within a transplanted organ is likely to be important to graft health and survival post-transplantation. We have previously shown that in the absence of immunosuppression, donor tissue-resident leukocytes are depleted following MHC-mismatched transplants, due to infiltrating recipient effector leukocytes. We hypothesised, therefore, that the retention of donor leukocytes described following mismatched transplants in humans is a result of immunosuppressive therapy, which targets recipient effector cells. In this study, we investigated the impact of different immunosuppressive agents as monotherapies on the retention of donor leukocytes after MHC-mismatched transplantation.

Methods: We developed immunosuppression regimens using clinically-relevant levels of immunosuppressive medications including tacrolimus and mycophenolate, and treated mice receiving MHC-mismatched kidney transplants. At seven days post-transplant, we compared the donor leukocyte retention and recipient leukocyte responses of mice on immunosuppression to those without.

Results: As expected after immunosuppression treatment, the circulating lymphocyte count was decreased. Simultaneously, the absolute number and proliferation of recipient lymphocytes within the graft and peripheral organs were reduced in comparison to immunocompetent controls. Immunosuppression also altered macrophage polarisation within the graft, to a less pro-inflammatory phenotype. Interestingly, our preliminary data showed that despite the decrease in recipient leukocyte infiltration, and a less inflammatory microenvironment within the graft, treatment with a single immunosuppressive agent did not improve donor leukocyte retention post-transplantation.

Conclusions: This highlights the requirement for the use of multiple immunosuppressive agents to sufficiently suppress recipient effector leukocyte responses, not only for graft tolerance but for donor leukocyte retention.


P2.14

Accelerating the Differentiation of Neonatal Porcine Pancreatic Cell Clusters Into Beta Cells in Alginate-Microcapsules

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Background: β-cell replacement is a promising strategy to treat type 1 diabetes. Neonatal porcine pancreatic cell clusters (NPCCs) have growth capacity after isolation, but immature to normalize blood glucose levels. We previously showed that NPCCs differentiate and expand in alginate-capsule. The aims of this study, we encapsulated NPCCs with alginate and accelerated NPCCs into beta cells using small-molecules. And then the differentiated NPCCs-capsules were transplanted in diabetic BALB/c mice.

Methods: NPCCs were isolated from 3 days old piglets. NPCCs were cultured for 5 days in Ham’s F-10 media and encapsulated with alginate on day 5. The microencapsulated NPCCs were divided by two groups; control, differentiation. DMEM/F-12 media was used as basal media for control group. For maturation of microencapsulated NPCCs, the media was supplemented with ALK5i, T3 and Exendin-4. Both groups were cultured for 2 weeks. The control and differentiated NPCCs (8,000 IEQ) were transplanted into type 1 diabetic BALB/c mice.

Results: The proportion of insulin-positive cells was greater in differentiation group than control group. Insulin mRNA levels and insulin secretion were significantly higher in differentiation group compared to control.

Conclusion: We have founded that the combination of ALK5i, T3 and Exendin-4 promoted the differentiation of immature NPCCs into beta cells.
A Positive B2 Microglobulin Trend Immediately After Transplant Identify Worse Outcomes in Patients With Delayed Graft Function

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**Background:** Delayed graft function (DGF) is associated with worse short and long-term outcomes after kidney transplantation. There is a lack of biomarkers to predict outcomes in patients with DGF. Serum β2 microglobulin is a low-molecular-weight protein that correlated with creatinine but it has the advantage of measuring residual renal function in dialysis patients. In kidney transplant patients, β2 microglobulin at the time of discharge is associated with graft failure and overall mortality. The role of the β2 microglobulin trend in patients with DGF has not been explored.

**Methods:** This is a retrospective study of deceased kidney transplant patients from 2013 to 2019. β2 microglobulin trend was defined as the difference between β2 on postoperative day four and β2 on postoperative day one. We used univariate and multivariate logistic regression models with level of significance of α=0.05.

**Results:** A total of 236 kidney recipients were reviewed, 105 (44.5%) had delayed graft function (median 9 days, 1 - 53); 50% of the patients with DGF received dialysis for one week only. The demographic and clinical characteristics of the patients with and without DGF is shown in table 1. β2 microglobulin significantly correlated with the presence of DGF (p<0.001) and significantly correlated with eGFR at 1, 3 and 6 months in all patients (p<0.001). In DGF group, β2 microglobulin trend correlated with the duration of DGF with p<0.05. This was independent of donors after circulatory death and type of kidney storage. In our cohort, β2 microglobulin was not associated with mortality or rejection.

**Conclusions:** The β2 microglobulin trend is a marker of kidney function useful particularly in patients with DGF, because measures the residual kidney function in the setting of dialysis. Following the trend of β2 microglobulin in patients with DGF is informative about the duration of the DGF and may help to make clinical decisions.

This study didn’t receive any funding.
P2.16
Influence of Immunosuppressive Drugs on NK Cells in Therapeutic Drug Exposure
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Background: Natural killer (NK) cells are enriched in lymphocytes within the liver and are considered to be main regulators of liver transplantation rejection and tolerance. However, the effects of immunosuppressants on NK cells are not clearly understood. The purpose of this study was to evaluate the impact of trough level conditions of immunosuppressants on NK cell function

Methods: Cytolytic activity of NK cells from primary PBMC to lyse K562 or HL60 cells was detected using the CFSE staining method. NK cells were exposed to single drugs [Everolimus(EVE), 5 ng/mL; Sirolimus(SIR), 5 ng/mL; Tacrolimus(TAC), 5 ng/mL; Cyclosporine A (CSA), 125 ng/mL; Mycophenolate Mofetil (MMF), 15 µg/mL; Steroid, 0.5 µg/mL; Group 2: TAC, 5 ng/mL + SIR, 5 ng/mL + Steroid, 0.5 µg/mL; Group 3: TAC, 5 ng/mL + EVE, 5 ng/mL + Steroid, 0.5 µg/mL] for 3 days as effector cells. The killing rate of NK cells was detected by flow cytometry.

Results:
1. Combined immunosuppressive therapy (Group1: TAC, 5 ng/mL + MMF, 15 µg/mL + Steroid, 0.5 µg/mL; Group2: TAC, 5 ng/mL + SIR, 5 ng/mL + Steroid, 0.5 µg/mL; Group 3: TAC, 5 ng/mL + EVE, 5 ng/mL + Steroid, 0.5 µg/mL) had the greatest impaired to NK cell killing function.
2. In comparison among single drugs, Steroid, MMF and mTOR inhibitor (EVE, SIR) have the strongest impaired to killing function. Interestingly, calcineurin inhibitors (TAC, CSA) had no significant effect on the killing function of NK cells. Compared with mTOR inhibitors, purine inhibitor MMF has better inhibitory effect, which can guide clinical medication.

Conclusions: This is the first time to use drug plasma concentration simulating the clinical microenvironment in stable liver transplant recipients under in vitro conditions. Exposure to immunosuppressants impaired the killing ability of NK cells in varying degrees. The inhibition effect of combination therapy is the strongest, followed by steroid, MMF and mTOR inhibitors, and steroid accounts for the main factor in combination therapy. In addition, as the first-line treatment after liver transplantation, calcineurin inhibitors have little effect on the killing ability of NK cells.

P2.17
Retrograde Reperfusion of the Renal Graft in Adult Recipient To Reduce Ischemia-Reperfusion Injury
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Introduction: Ischemic reperfusion injury (IRI) of a kidney graft is still a current problem in transplantology. The aim of research was study of the effect of retrograde venous renal transplant reperfusion (RVR) on the reduction of IRI in kidney transplant.

Materials and methods: There are seven kidney transplantations in adults from a living donor performed using RVR. Retrospectively analyzed eight recipients’ medical records with typical arterial reperfusion (without RVR). After the standard laparoscopic donors’ nephrectomy, the renal graft was washed with a solution of “HTK” with heparin. After applying an end-to-side venous anastomosis, arterial anastomosis applied. At the same time, RVR with venous blood performed. About 80-100ml of retrograde venous blood flowed from the opening renal transplant artery. Then a typical antegrade reperfusion followed. Immunosuppression was a three-component: CNI + MMF + Steroid with Basiliximab induction in both group. Blood perfusate from the kidney artery collected for blood gas analysis; 1st day diuresis, creatinine and urea analyzed on the 4th and 30th days after surgery and compared with control group. Immunosuppression was a three-component: CNI + MMF + Steroid with Basiliximab induction in both group. Blood perfusate from the kidney artery collected for blood gas analysis; 1st day diuresis, creatinine and urea analyzed on the 4th and 30th days after surgery and compared with control group. Immunosuppression was a three-component: CNI + MMF + Steroid with Basiliximab induction in both group. Blood perfusate from the kidney artery collected for blood gas analysis; 1st day diuresis, creatinine and urea analyzed on the 4th and 30th days after surgery and compared with control group.

Results: In all cases, the graft function was satisfactory. There were no vascular complications. Significant changes in pH, PO2, BEEcf, HCO3−, Lac, K+, and Ca2+values observed in retrograde blood. In the RVR-group daily diuresis in first POD, there was no polyuria, while in the control group there was significant polyuria. Normalization of serum creatinine and urea levels observed on average on the 4th day after surgery (Table 1 and 2).

Conclusion: The results of the initial experience of kidney transplantation using RVR show an improvement in the function of the kidney transplant. In the future, an increase in the cohort of patients is required to study the effect of RVR.

Table 1. Comparative data of two groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1-group with RVR (n = 7)</th>
<th>2-group without RVR (n = 8)</th>
<th>r*</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Initial Creatinine</td>
<td>672 ±162</td>
<td>615.0 ±155.8</td>
<td>0.1297</td>
<td>0.19499</td>
</tr>
<tr>
<td>Initial Urea</td>
<td>10 ±6.7</td>
<td>10.0 ±3.1</td>
<td>0.05915</td>
<td>0.553733</td>
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<tr>
<td>Initial e-GR</td>
<td>10 ±2.0</td>
<td>10.0 ±2.6</td>
<td>0.26585</td>
<td>0.79599</td>
</tr>
<tr>
<td>Creatinine POD04</td>
<td>77.27 ±46.3</td>
<td>100.0 ±44.2</td>
<td>8.08979</td>
<td>&lt; 0.00001</td>
</tr>
<tr>
<td>Urea POD04</td>
<td>7.34 ±1.9</td>
<td>10.19 ±1.1</td>
<td>2.44873</td>
<td>0.023775</td>
</tr>
<tr>
<td>Creatinine POD030</td>
<td>46.80 ±67.4</td>
<td>85.25 ± 4.6</td>
<td>5.07515</td>
<td>0.003214</td>
</tr>
<tr>
<td>Urea POD030</td>
<td>6.4 ±1.0</td>
<td>8.25 ±0.5</td>
<td>4.74208</td>
<td>0.000197</td>
</tr>
<tr>
<td>Daily diuresis POD01</td>
<td>4650 ± 934</td>
<td>9544 ± 2226.5</td>
<td>5.39443</td>
<td>0.000122</td>
</tr>
</tbody>
</table>

* The Student’s t-test used. RVR: Retrograde Venous Reperfusion. e-GR: estimated Glomerular Filtration Rate. POD: Postoperative Day.

Table 2. Retrograde blood gas analyses.

<table>
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<tr>
<th>Parameter</th>
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<th>BEEcf</th>
<th>Lactate</th>
<th>PO2</th>
<th>K+</th>
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<td>-26.7</td>
<td>4.3</td>
<td>52</td>
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<tr>
<td>02</td>
<td>6.72</td>
<td>-26.9</td>
<td>4.8</td>
<td>59.2</td>
<td>16.1</td>
<td></td>
</tr>
<tr>
<td>03</td>
<td>6.7</td>
<td>-27.3</td>
<td>4.9</td>
<td>54.5</td>
<td>14.2</td>
<td></td>
</tr>
<tr>
<td>04</td>
<td>6.7</td>
<td>-27.5</td>
<td>5.2</td>
<td>53.1</td>
<td>13.5</td>
<td></td>
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<tr>
<td>05</td>
<td>6.699</td>
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<td>6.72</td>
<td>-26.9</td>
<td>4.8</td>
<td>59.2</td>
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</table>
Local Immune Cells' Phenotype After Corneal Graft Rejection

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Introduction: Penetrating keratoplasty is a vision-saving procedure. It is relatively easy to perform, as it does not require immunological matching, yet the grafts survival rates are high. The risk of graft failure increases in the case of repeated transplantation. The possible reason is that alloimmunization and subsequent immunological rejection prime the adaptive immune system for the next mismatched tissue. The rejection process, described generally on a mouse model, is mediated by CD4+ T cells, however, other populations of immune cells were also reported. This study aimed to characterize cells present in the rejected corneas of human patients qualified for retransplantation.

Methods: In the study, we analyzed cells isolated from explanted corneas from patients qualified for corneal transplantation (TX), either first procedure (primary TX, PTX group n=13) or retransplantation (repeated TX, RTX group n=13). The tissue was incubated for 24h in a culture medium at 37°C to allow immune cells to release from the tissue. For comparison, peripheral blood (PB) was acquired. The samples were analyzed by flow cytometry for lineage markers of T, B, and NK cells, T regulatory cells (Tregs), memory phenotype (CD62L, CD45RA), and Helios expression.

Results: Figure 1 presents representative cytograms of cells isolated from cornea tissue. The most abundant population of mononuclear cells in the cornea was T cells (median=54,4%), with a negligible level of B cells (median=0,55%). Both CD4+ and CD8+ T cells were present in proportion comparable to peripheral blood, in both groups. There was a significantly more effector memory CD4+ (PTX Me=80,3%; RTX Me=61,9%; p=0,04) and CD8+ (PTX Me=83,3%; RTX Me=74,4%; NS) T cells within the tissue than in PB. The lower level of effector memory cells in RTX group was compensated with increase in central memory compartment. Tregs were detected in both groups in similar proportion to PB (Me=7,0% in cornea and Me=6,5% in PB). Tregs present in the cornea seems to have a low proportion of Helios positive cells with the median of Helios+ to Helios- Tregs 1:2. Interestingly, the PTX group showed a higher percentage of Helios+ Tregs in corneal infiltrate compared to the RTX group (p= 0,0254).

Conclusion: Corneas explanted from human patients present a mixed infiltration of immune cells. Both rejection process and primary corneal diseases facilitate immune cells infiltration into the tissue. T cells are generally the effector memory phenotype suggesting activation of the adaptive immune response, moreover, rejection of the allograft is associated with a higher proportion of central memory T cells. Within the tissue Tregs are present, however, low expression of Helios transcription factor suggests their instability. Understanding the immune status of primary corneal diseases may improve evaluation of allograft rejection risk while understanding the process of rejection will allow for a better management of transplant patients.

The study was supported by the project POWR.03.05.00-00-z082/18 co-financed by the European Union through the European Social Fund under the Operational Programme Knowledge Education Development 2014–2020.
Role of the Intestinal Microbiota in the Course of Chronic Liver Disease Before and After Liver Transplantation Results of A Pilot Study

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Introduction: Since the moment the article “Our Other Genome”, clearly presenting the genetic catalog of the human gut microbiota, had been published in the journal “Nature”, views of the scientific community on the etiology of chronic liver diseases (CLD) have changed significantly. A large number of recently published studies have been dedicated to the intestinal microbiota in patients with hepatocellular carcinoma (HCC) and alcoholic liver disease as well as the degree of influence of the intestinal microbiota on the course of CLD. However, results of these studies have been quite different. In this regard, we have started our own prospective cohort study of the intestinal microbiota in patients with CLD.

Methods: Our prospective study was based on evaluation of 12 patients suffering from liver cirrhosis and HCC on the background of liver cirrhosis while being on the waiting list for a liver transplantation. Patients were divided into two groups accordingly. In order to determine the gut microbiome palette, the 16s RNA NGS was used. Stool samples were collected 24 hours before, 72 and 168 hours after liver transplantation. The average MELD score within the liver cirrhosis group was 15 (6-30 points). HCC in patients of the second group was within the Milan criteria.

Results: The results of our study showed the absence of any statistically significant difference in the gut microbiota palette of patients with liver cirrhosis of different Child-Turcotte-Pugh functional classes as well as the MELD score (p>0.05) (Fig. 1). Moreover, we did not observe any significant difference in the gut microbiome palette in patients after liver transplantation who were initially referred to different Child-Turcotte-Pugh functional classes (p>0.05). However, in the post-transplant period, Proteobacteria were replaced by Bacteroides in patients of the liver cirrhosis group. Besides, in the long-term period after liver transplantation, we noted some difference in the microbiome palette in patients of different functional classes of severity (Fig. 2). At the same time, we noted a pronounced difference in the taxometric picture of the gut microbiome in the post-transplant period in a patient with developed acute cellular rejection.

Conclusion: Since our study was of a pilot nature, its disadvantage may be a small number of studied patients. However, the obtained results indicate the absence of a specific effect of the microbiota on the natural course of liver cirrhosis, even in patients with pronounced liver decompensation (MELD 30). With that said, the revealed microbiome difference in patient with an acute cellular rejection of the graft indicates a dramatically important role of the intestinal microbiota in the development of this complication. In this regard, the obtained data indicate potential significance and expediency of further research in this direction.
Angiogenesis Promoting Effects of Human Amnion Membrane in Ischemia-Impaired Wound in a Rat Model

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Background: Ischemic wounds are intractable and require revascularization for healing. However, many patients with ischemic wounds have serious comorbidity, and revascularization surgery is not necessarily applicable for those patients, resulting in amputation of the lower limbs. Therefore, it would be useful to establish wound dressing materials with revascularization effects. Human amniotic membrane (hAM) has a variety of characteristics that make it potentially useful as a wound dressing material. However, there have been few reports on the angiogenesis promoting effects of hAM in ischemia-impaired wound. The aim of this study was to examine the efficacy of hAM as a wound dressing material for ischemic wounds.

Methods: Amniotic membranes were collected from delivered placenta with the consent of a pregnant woman who underwent a cesarean section. Fresh hAM were used within 6 hours of collection. Ischemic wounds were made at abdominal wall of male rats (SD, 9 weeks old, 300-350 g) by ligating the arteriovenous and nerve bundles of inferior abdominal wall and excising the abdomen skin with a diameter of 2.0 cm. Microvessel density (MVD) as an index of angiogenesis was measured by double staining with anti-α-SMA and anti-CD34 antibodies. The density of the number of blood vessels as well as the wound area were compared between hAM group and control group.

Results: The wound area after 5 days was significantly smaller in hAM group than in control group (335 vs. 459 mm², p = 0.0051). The mean value of MVD was significantly higher in hAM group than in control group (19.0 vs. 15.1, p = 0.0026). Histological evaluation showed no obvious rejection of the hAM in this study.

Conclusion: This study showed the wound healing effect and the angiogenesis promoting effect of fresh hAM, indicating the usefulness of fresh hAM for treating non-invasively ischemic wounds.

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P2.21

Protection of Normal Metabolic Function of Healthy Pig Livers Following Prolonged Normothermic Ex-situ Perfusion

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Introduction: For end-stage liver diseases, liver transplantation remains the most suitable therapy for its treatment. Nonetheless, the current gap between the patients on the waiting list and the graft supply, as well as the gold standard preservation method (Static Cold Storage or SCS), limits its usefulness. Extended Criteria Donors (ECD) has been proposed as a potential solution to increase the donor pool, although these have a greater susceptibility to ischemia-reperfusion injury (IRI), especially after SCS, causing delayed graft function and primary non-function. These side effects have fueled research into more suitable methods such as ex-situ normothermic machine perfusion (NMP).

Methods: Sixteen healthy pig livers were subjected to normothermic perfusion using blood as a perfusion solution. In 5 experiments, taurocholic acid was administrated 6 hours after perfusion initiation. Perfusate and bile were sampled before, during and after perfusion to assess the hepatocellular and liver function and bile duct injury and bile production. Liver samples were collected before and after perfusion to perform analysis of general damage, stellate cell activation, oxidative stress and LSEC response.

Results: AST and LDH levels increased progressively for the first 12 hours (P<0.02 and P<0.001 respectively). Afterward, both parameters stabilized. Glucose and lactate levels decreased rapidly during the first 4 hours (p=0.003 for glucose and p=0.04 for lactate) and reached the lowest within 8 (p<0.001) and 12 hours (p<0.001) respectively. Overall, blood pH remained steady (p=0.10). Serum levels of ALKP, GGT and Bil didn’t suffer any changes during all the perfusion (p=0.99, p=0.75 and p=0.13 respectively). Bile production started within 1 hour after ex-situ perfusion. Livers supplied with taurocholic acid had a higher bile production rate, 9±3 mL/h, compared to those not supplied, 4±3 (p=0.005). No structural alterations were detected in liver samples after the Suzuki injury score assessment (p=0.33) and stellate cell activation quantification by both gene (p=0.64) and protein expression (p=0.79) and percentage of the stained area (p=0.15). Although eNOS gene and protein expression increased (p=0.01 and p=0.008 respectively); histological analysis of CD31 endothelial staining showed no differences between the baseline, 35±9.1 %, and the 24-hour perfusion 36.3±7.2%, of the sinusoidal area (p=0.87). This increase was associated with higher levels of MDA after the perfusion (p=0.006) as the KLF2 gene and protein expression remained invariable (p=0.80 and p=0.26 respectively).

Conclusion: Our results show that NMP, as a preservation method, is capable of maintaining the normal hepatic structure and, at the same time, supporting normal metabolic activity. However, further studies should be conducted to demonstrate post-transplant liver viability.

P3.01

Similar Graft-Versus-Host Disease (GVHD) Incidence Among Unrelated and Identical Sibling Donor Transplantation With the Use of Anti-thymocyte Globulin (ATG)

Agustina Caia1, Martin m Castro2, Alejandro Requejo1, Nicolas Fernandez Escobar1, Gonzalo Bentolilla1, Gregorio Jaimovich1,2, 1Bone Marrow Transplantation Programme, Favaloro University Hospital, Caba, Argentina; 2Bone Marrow Transplantation Programme, Sanatorio Anchorena, Caba, Argentina; 3Bone Marrow Transplantation Programme, Fundaleu, Caba, Argentina.

Introduction: GVHD is the main cause of morbidity and mortality associated with allogeneic hematopoietic stem cell transplantation (HSCT) with an incidence rate of 40-60%. Addition of ATG has shown to reduce its incidence. We report the GVHD outcomes with the use of ATG as part of the prophylaxis regimen in a group of patients (pts) undergoing HSCT.

Methods: From March 2018 to June 2021 we conducted a prospective multicenter study including 95 consecutive pts.: 33 transplanted with an identical sibling donor (ISD), 33 with an HLA-matched unrelated donor(MUD) and 18 with an HLA 1 miss-matched donor (MMUD). Conditioning regimen was according to institutional protocol. GVHD prophylaxis included tacrolimus and methotrexate plus ATG (Timoglobulina®Sanofi) 2.25 mg/kg days -3 and -2.

GVHD incidence, relapse and death were recorded. Acute GVHD (aGVHD) and chronic GVHD (cGVHD) were defined according Glucksberg criteria and NIH clinical grading respectively. Median and interquartile range (IQR) were used to describe non-parametric data, group comparison with X2, Kaplan Meyer curve and multi-sample log Rank test for survival analysis, considering a statistically significant p value of less than 0.05.

Results: 42 pts were male and donors were female in 56% (n:54). Conditioning regimen was myeloablate in 81% (n:77). Median time to neutrophil and platelet engraftment were 17 days (range 15-21) and 17 days (range 12-20) respectively. 6/95 pts presented graft failure. aGVHD incidence was 36% (n:34). grades I-II 19% (n:19) and III-IV 16% (n:15). Incidence of grades III-IV did not varied according to donor: 15% (n:7) for ISD, 9% (n:3) for MUD and 27% (n:5) for X2 3.06, p=0.21). Overall incidence of cGVHD was 23% MMUD (n:21); Grades mild 6% (n:6), moderate 11% (n:11) and severe 4% (n:4). According to donor type, severe cGVHD was 2% (n:1), 3% (n:1) and 11% (n:2) using ISD, MUD and MMUD respectively (X2 2.65, p=0.26).

At one year, 15/79 pts (19%) were under immunosuppressive treatment. Transplant related mortality at day 100 was 9% (n:9). Most frequent cause was sepsis (n:4). In 31 pts CMV reactivation was detected (more than one reactivation in 6 pts of which 5 had GVHD) and 7 reactivated EBV infection. None evolved to PTLD.

Median follow-up time was 524 days (IQR 168-833). cGVHD-free and relapse-free survival (combined endpoint) at 1 year was 57% (n:54) of 79 evaluable patients. cGVHD and relapse free survival at 1 year was 48% for HLA-33-63%CI), 66% for MUD (47-81%CI) and 38% for MMUD (21-60%CI). No significant difference was found according to donor type (X2 4.98; p=0.083).

Conclusion: With the use of ATG no difference was observed in the incidence of aGVHD grades III-IV and severe cGVHD between the different types of donor. This results should be confirmed with a higher level of evidence study.

<table>
<thead>
<tr>
<th>ISD (n:44)</th>
<th>MUD (n:33)</th>
<th>MMUD (n:18)</th>
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</thead>
<tbody>
<tr>
<td>aGVHD</td>
<td></td>
<td></td>
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<tr>
<td>Total, n (%)</td>
<td>12 (27%)</td>
<td>15 (46%)</td>
</tr>
<tr>
<td>III-IV, n (%)</td>
<td>7 (16%)</td>
<td>3 (9%)</td>
</tr>
<tr>
<td>p NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cGVHD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total, n (%)</td>
<td>9 (20%)</td>
<td>6 (18%)</td>
</tr>
<tr>
<td>Severe, n (%)</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>p NS</td>
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</table>
Assessment of Chimerism Testing by Next Generation Sequencing

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Introduction: Chimerism analysis of recipient and donor cells enables the assessment of engraftment, minimal residual disease, and early detection of relapse post hematopoietic stem cell transplantation (HSCT). This is the first study to evaluate the use of two novel multiplex next generation sequencing (NGS) chimerism assays.

Methods: DNA extracted from peripheral blood samples with known mixed chimerism percentages were used in two multiplex NGS chimerism assays following manufacturer’s instructions to assess accuracy, reproducibility, lower limits of detection of chimerism. DNA sequencing was performed on the Illumina MiSeq system and analysis was completed using the associated manufacturer software.

Results: Chimerism assay 1 (Devyser) utilized 10/24 informative markers and the lower limit of detection was 0.1%. Chimerism assay 2 (GenDx) utilized 17/32 informative markers and the lower limit of detection was 0.5%. Both assays demonstrated excellent comparable accuracy and reproducibility throughout all tested chimerism ratios.

Conclusion: High sensitivity chimerism assays using NGS technology may allow better quantitative monitoring of engraftment post HSCT compared to the current gold standard short tandem repeat-based PCR with capillary electrophoresis (STR PCR CE) method.
P3.03

Allogeneic Hematopoietic Stem Cells Transplantation (AH SCT). Is Still the Sibling Donor the Best Option? One Single Center Experience

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Objectives: To determine: Incidence and severity of acute GVHD according to the type of donor, their age and/or the source of hematopoietic progenitor cells (HPC). MRT according to type of donor and age range Incidence and extension of chronic GVHD according to type of donor, age and/or source of CPH.

Materials and methods: Prospective study comparing the results in 161 (pediatric and adults) correlative patients undergoing HSCT between May 2015 and August 2020, establishing 4 cohorts according to the donor:

- HLA-identical related transplant (MSD) (n = 45) (26 adults and 19 pediatric).
- HLA-identical unrelated transplant (HAPLO) (n = 36) (19 adults and 17 pediatrics).
- HLA-identical unrelated transplant (MUD) (n = 51) (20 adults and 31 pediatrics).
- Unrelated transplant with 1 mismatch (MMUD) (n = 29) (14 adults and 15 pediatrics).

Results: Diagnosis: AML-MDS: 36% (n: 59), ALL 27 (n: 44) aplastic anemia: 8% (n: 14) 8% (n: 13) primary immunodeficiency (ID) and others. The most frequent diagnosis in pediatrics was ALL and in adults AML - MDS. 13 of 79 adults were older than 60 years (16%). The source of CPH was bone marrow (BM) in 68 patients (42%) and peripheral blood (PB) in 93 (58%). In pediatrics, 79% used MO and in adults, 91% SP. The incidence of acute GVHD varies according to the type of donor used, as assessed in table 1. There are no significant differences in the incidence of acute GVHD comparing the source of CPH (MO versus SP) nor the pediatric versus adult population. The MRT also varies according to the type of donor, as can be seen in table 1.

Conclusions: Acute leukemias are the main indication for allogeneic HSCT in both the pediatric population and the adult population. Bone marrow as a source of CPH is the most frequent option in pediatrics, while SP is in adults. HSCT with MSD is the one associated with the lowest incidence of acute GVHD, followed by MUD.

P3.04

Apraglutide Treatment Reduces Chemotherapy-Induced Gastrointestinal (GI) Damage in Mice and Preserves Cellular Integrity During Chemotherapy

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1Translational Science, VectivBio, Basel, Switzerland; 2Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada

Background: Chemotherapy-induced mucositis is a common condition caused by the breakdown of the mucosal barrier. Administration of exogenous glucagon-like peptide 2 (GLP-2) has been associated with reduced epithelial damage, decreased bacterial infection, and decreased mortality or gut injury in rodents with chemically induced enteritis. GLP-2 decreases chemotherapy-induced mucositis via inhibition of drug-induced apoptosis in the small and large bowel. Apraglutide is a novel, long-acting synthetic GLP-2 agonist that has been shown to promote intestinal growth and repair. Two preclinical studies aim to evaluate the efficacy of apraglutide (2.5 mg/ kg) as pre-treatment or concomitant treatment in models of chemotherapy-induced intestinal damage with cytarabine or melphalan; both extensively used in hemat-oncology.

Methods: Study 1 included four groups of Balb/c mice: (A) vehicle only; (B) cytarabine on Days 5-9, no apraglutide given; (C) cytarabine on Days 5-9; concomitant apraglutide on Days 5-18; (D) cytarabine on Days 5-9; pre-treatment apraglutide on Days 1, 3, 5, and continued as a concomitant treatment on Days 5, 8, 11, 14, and 17. Study 2 included three treatment groups of Balb/c mice: (A) vehicle only; (B) melphalan on Day 9, no apraglutide; (C) melphalan on Day 9; pre-treatment apraglutide on Days 1, 3, 5, 7 and continued as a concomitant treatment on Days 9, 11, and 13. In both models, mice that received the vehicle without any treatment served as controls. Intestinal tissue histology, body weight, survival, and plasma citrulline, a marker of total mucosal mass and intestinal growth, were assessed in both models.

Results: Histological examination showed that the degenerative intestinal changes (villi and crypt atrophy) caused by cytarabine or melphalan were reduced by apraglutide co-administration, as demonstrated by similarities in tissue morphology between vehicle-treated and apraglutide-treated mice. In addition, the duodenum, ileum, and jejunum increased in weight with apraglutide. The intestinal protective effects of apraglutide were further supported by preserving plasma citrulline levels (a biomarker of intestinal mass); apraglutide-treated mice had similar levels to animals that did not receive chemotherapy. Apraglutide attenuated chemotherapy-induced weight loss and improved overall survival vs. vehicle-only or chemotherapy-only groups. The effects of apraglutide were optimal when it was administered as pre-treatment before chemotherapy.

Conclusion: Microscopic examination showed apraglutide protected GI epithelium structure from chemotherapy-induced injury, improved survival, and prevented severe body weight loss in mice undergoing chemotherapy. Apraglutide also maintained plasma citrulline levels, a marker of intestinal mass, comparable mice that did not undergo chemotherapy.
Apraglutide Decreases Severity of Intestinal Damage From Acute Gastrointestinal Graft Versus Host Disease (GI-GvHD) Following Allogeneic Transplantation Without Impacting Engraftment

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1Translational Science, VectivBio, Basel, Switzerland; 2Centre de recherche de l’Hôpital, Maisonneuve-Rosemont Hospital, Montréal, QC, Canada; 3Département de microbiologie, infectiologie et immunologie, Université de Montréal, Montréal, QC, Canada; 4Département de médecine, Université de Montréal, Montréal, QC, Canada; 5Institut Universitaire en Hématologie Oncologie et Thérapie Cellulaire, Hôpital Maisonneuve-Rosemont - CIUSSS-EMTL, Montreal, QC, Canada

Background: The GI tract is a primary tissue system damaged by GvHD, leading to a compromised mucosal barrier, mucosal protein loss, and nutrient/fluid absorption failure. Glucagon-like peptide-2 (GLP-2) has demonstrated intestinotrophic effects, enhanced barrier function, and decreased intestinal permeability. Apraglutide, a novel, long-acting synthetic GLP-2 analog, represents a potential regenerative approach to GI GvHD prevention and treatment. Using two mouse models of GvHD, we assessed the effects of apraglutide on engraftment and GI protection following irradiation and allogeneic transplantation.

Methods: In Study 1, total-body-irradiated (TBI) immunodeficient (NOG) mice (Day 0) were injected with human peripheral blood mononuclear cell (hPBMC; 3x10^7; Day 2) and treated with apraglutide 3.3 mg/kg or vehicle (Days -6 to 18). Engraftment rate was determined through CD45 expression (human vs. mouse) in blood, bone marrow, and spleen. In Study 2, TBI-induced intestinal damaged BALB/cJ mice received allogeneic transplantation from C57BL/6 strain and were treated with apraglutide (3.3mg/kg) or vehicle (Days -9, -7, -5, -3, -1, +1, +3, +5, +7). Intestinal damage indicative of GvHD (histological changes, length, hemorrhage, inflammation), body weight, and survival were assessed.

Results: In study 1, hPBMC were successfully engrafted. The engraftment rate in blood, spleen, and bone marrow was not affected by apraglutide (range 22.2-47.6% at D20 in blood). hCD45+ cell infiltration was observed in the intestinal wall with no difference between apraglutide vs. vehicle. In study 2, lymphocyte engraftment was successfully achieved in both apraglutide- and vehicle-treated mice. Weight loss and median survival were similar in both groups, but apraglutide-treated mice had significantly higher overall survival vs. vehicle on Day +9 (40% vs. 0%, respectively; p=0.0134). Post-mortem histological examination revealed less mucosal degenerative/inflammatory changes (villous atrophy, mononuclear/neutrophilic cell infiltrate in the lamina propria/extra-cryptal epithelium, crypt necrosis) in apraglutide-treated mice vs. vehicle. Mean colon length in the apraglutide group (8.6±0.35 cm) was comparable to mice that did not undergo irradiation or transplantation (9.6±0.33 cm), whereas a significant reduction was apparent in the vehicle group (7.19±0.10 cm; p <0.05).

Conclusion: These results suggest that apraglutide treatment before allogeneic transplantation in immunodeficient mice does not affect engraftment rate. Furthermore, apraglutide showed a significant protective effect in TBI- and allogeneic-transplant-induced GvHD with reduced villi atrophy, less colon shortening, less severe intestinal damage, and showed a survival advantage. These findings support the beneficial role of apraglutide in reducing GI damage and limiting mortality from GvHD.

Figure 1: Apraglutide has no impact on engraftment of human PBMC in NOG irradiated mice
Abstracts

P3.06
Apraglutide Does Not Impact Anti-tumor and Immunosuppressive Efficacy of Conditioning Chemotherapy in Mice

Violetta Dimitriadou1, Mark Minden2.
1Translational Science, VectivBio, Basel, Switzerland; 2Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada

Background: Conditioning chemotherapy reduces tumor burden and provides immunosuppression to prevent graft rejection with hematopoietic cell transplantation, but often induces mucosal barrier breakdown and mucositis. Apraglutide is a novel, long-acting synthetic glucagon-like peptide-2 (GLP-2) analog that protects the GI epithelium from chemotherapy-induced injury, improves survival, and allows better weight maintenance in mice undergoing chemotherapy. Preclinical studies aim to evaluate the impact of apraglutide on chemotherapy’s efficacy in reducing tumor load and inducing immunosuppression.

Methods: Study 1 assessed cytarabine’s antitumor effects in leukemic NOD/SCID mice. Apraglutide or vehicle was administered on Days -4 to 4. Cytarabine or vehicle was administered on Days 0-4. Bone marrow and spleen samples were collected on Day 7, and the percentage of hCD45+ cells was determined. Study 2 assessed the effect of apraglutide on cytarabine-induced immunosuppression and included three groups of Balb/c mice: (A) vehicle; (B) cytarabine on Days 5-9; (C) cytarabine on Days 5-9, concomitant apraglutide on Days 5-13. RBC, platelets, WBC, NEU, and LYMPH, were assessed. A cohort was allowed to survive for four weeks to evaluate the effect of apraglutide on immunosuppression recovery. Study 3 assessed the effect of apraglutide on melphalan-induced immunosuppression. Three groups of Balb/c mice were included: (A) vehicle; (B) melphalan on Day 9; (C) melphalan on Day 9, apraglutide pre-treatment on Days 1, 3, 5, 7 and continued as co-administration on Days 9, 11, and 13. WBC, NEU, and LYMPH were assessed.

Results: Study 1 showed that human leukemia cells reduction did not differ significantly between cytarabine-only and cytarabine + apraglutide and were significantly greater than in the vehicle-only group. The percentage of hCD45 in bone marrow after chemotherapy was 35.5±4 with cytarabine-only and 33.9±4.2 with cytarabine + apraglutide. A dramatic decrease in leukocytes at the end of the treatment period in Study 2 indicated that cytarabine-induced immunosuppression was not impaired by apraglutide co-administration (91% reduction in lymphocytes with both cytarabine + apraglutide and cytarabine-only). Apraglutide did not impact the recovery of hematological parameters four weeks after the end of treatment. Study 3 showed that melphalan elicited immunosuppression as evidenced by leukocyte decrease. Mice treated with melphalan, with or without apraglutide, had severe reductions in WBC and LYMPH vs. vehicle.

Conclusions: Pre- and concomitant apraglutide did not impair the efficacy of cytarabine in destroying human leukemia cells in vivo. Moreover, combination with apraglutide had no negative impact on cytarabine- or melphalan-induced immunosuppression. Apraglutide did not negatively impact the antitumor or immunosuppressive effects of cytarabine or melphalan.

Blood cell count

<table>
<thead>
<tr>
<th>Blood cell count</th>
<th>Percentage difference from control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cytarabine only at treatment end</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>-35</td>
</tr>
<tr>
<td>Platelets</td>
<td>-48</td>
</tr>
<tr>
<td>White blood cells</td>
<td>-68</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>-91</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>-42</td>
</tr>
</tbody>
</table>

*Administered 3 days before start of cytarabine treatment; 0 days after end of cytarabine treatment
P3.07

Treatment With Apraglutide Preserves the Global Homeostatic Environment of Intestinal Microbiota During Chemotherapy in Mice

Violetta Dimitriadou1.
1Translational Science, VectivBio, Basel, Switzerland

Background: Hematopoietic stem cell transplantation patients experience profoundly altered gut microbiota composition due to dysregulation of intestinal homeostasis by conditioning regimens, broad-spectrum antibiotics, immunosuppressants, and the introduction of foreign lymphocytes from the donor. A growing body of evidence shows reduced microbiome diversity increases the incidence and seriousness of graft versus host disease (GvHD) and bacteremia. Apraglutide, a novel long-acting synthetic glucagon-like peptide 2 (GLP-2), has been shown to protect gastrointestinal (GI) epithelium structure from chemotherapy-induced injury, improve survival, and allowed better body weight maintenance in mice undergoing chemotherapy. The study aimed to evaluate the protective effect of apraglutide on gut microbiota during chemotherapy with cytarabine.

Methods: Balb/c mice received 30 mg/kg of cytarabine on Days 5-9 and apraglutide 3.3 mg/kg on Days 1-18. Control mice received the vehicle on Days 1-18. Fecal samples were collected over 24 hours for bacterial phenotyping at pre-treatment and the day before scheduled termination and for found dead or pre-terminally euthanized animals. Microbiota composition was determined by 16S taxonomical meta-sequencing.

Results: Bacteroidetes and Firmicutes were the two leading bacterial phyla identified. Chemotherapy with cytarabine caused significant changes in the composition of bacterial species, increasing the Bacteroidetes population and decreasing the proportion of Firmicutes bacteria. The change in Bacteroidetes and Firmicutes bacteria levels from Days 0 to 18 was significantly greater in the cytarabine-only and cytarabine + apraglutide mice vs. vehicle. However, this effect was reduced by apraglutide co-administration. The difference in the change between cytarabine-only and cytarabine + apraglutide groups reached statistical significance for both Bacteroidetes (0.2486; p<0.0001) and Firmicutes (0.2037; p<0.0001). In addition, the ratio of Bacteroidetes to Firmicutes bacteria present remained more constant in cytarabine + apraglutide than in the cytarabine-only group.

Conclusions: Chemotherapy profoundly impacted bacterial homeostasis in the mouse intestine, with a notable increase in opportunistic pathogenic bacteria populations. The proportions of different bacterial phyla in feces remained closer to normal when apraglutide was co-administered with chemotherapy. Treatment with apraglutide resulted in the preservation of the global homeostatic environment of the intestinal microbiota. Prevention of intestinal dysbiosis may contribute to the improved outcomes (reduced body weight loss, increased survival) observed in mice when apraglutide is administered concomitantly with chemotherapy agents.
P4.01

**Searching New Donation Scenarios: Potential Receptors “on the Other Side of the Mirror”**

Paula Rivera Sánchez1, Jose Moya Sánchez1, Clara Manso Murcia1, Nayara López Hernández1, María Granados Madero1, Mario Royo-Villanova Reparaz1, Tamara Puche Bolarín1, María Dolores Victoria Ródenas1, Mónica Valer Rupérez1, María del Mar Martín Magán1, Ramón Mula Martínez1, Marta Mateos Llosa1. 1Servicio de Medicina Intensiva, Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain.

**Introduction:** Advances in the field of extracorporeal circulation have improved the prognosis and survival of patients in situations of respiratory failure or cardiogenic shock. However, due to disease progression or not considering the inclusion on the waiting list, the purpose of extracorporeal support treatment may be considered futile. These patients who were waiting for an organ can become new donation scenarios, placing a potential receptor just “on the other side of the mirror”. The descriptive study analyzed the potential receptor of a thoracic organ with extracorporeal assistance who become donors in controlled asystole.

**Methodology:** Retrospective observational study of those donors who met the aforementioned criteria from January-2016 to September-2021 in a tertiary care hospital. Demographic, clinical, organ traceability, and donation effectiveness variables were collected.

**Results:** 9 real donors were collected. 77.8% were men with a median age of 56 years. 55% had some cardiovascular risk factor. The mean ICU stay was 12.1 days. 7 patients carried veno-arterial ECMO due to: postinfarction cardiogenic shock (4), pulmonary thromboembolism (1), primary heart transplant failure (1), and non-ischemic dilated cardiomyopathy (1). 2 patients with veno-venous ECMO due to pulmonary fibrosis pending transplantation. 19 organs were obtained (7 livers and 12 kidneys), which represents a ratio of 2.1 organs per donor and an effectiveness of 88.9%.

**Conclusion:** The shortage of donors forces us to broaden the search for new scenarios of donation. Although this type of “mirror” donor represents a significant change in treatment and emotional stress for their families, it is a source to consider once their care team considers the adequacy of life-sustaining treatment.

P4.02

**Performance of the Hypotension Prediction Index in Living Donor Liver Transplant Recipients: A Prospective Observational Study**

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**Background:** The hypotension prediction index (HPI), derived from various features of the arterial waveform, was recently introduced and clinically validated in various surgical conditions.

**Objective:** To evaluate the performance of HPI in living donor liver transplantation recipients.

**Design:** Prospective observational study.

**Setting:** Tertiary hospital, Republic of Korea, from August 2021 to January 2022.

**Patients:** Twenty adult patients undergoing living donor liver transplantation were enrolled.

**Intervention:** HPI was monitored via a radial artery catheter during liver transplantation.

**Main outcome measures:** The mean arterial pressure and HPI were recorded from the end of anaesthetic induction until the end of surgery at 1-minute intervals. The area under the curve (AUC) of the receiver operating characteristic curve was calculated to show the performance of HPI at 5, 10, and 15 min for the whole dataset and in each phase of liver transplantation.

**Results:** The AUCs for predicting hypotension in the consecutive 5, 10, and 15 min were 0.810 (95% confidence interval [CI]: 0.802–0.818), 0.726 (95% CI: 0.716–0.735) and 0.689 (95% CI: 0.679–0.699), respectively. In the prehepatic phase, the AUCs in the 5-, 10-, 15-min windows were 0.795 (95% CI: 0.780–0.810), 0.694 (95% CI: 0.677–0.711), and 0.626 (95% CI: 0.608–0.645), respectively. In the anhepatic phase, the AUCs in the 5-, 10-, 15-min windows were 0.728 (95% CI: 0.706–0.749), 0.672 (95% CI: 0.649–0.694), and 0.683 (95% CI: 0.660–0.705), respectively. In the neohepatic phase, the AUCs in the 5-, 10-, 15-min windows were 0.837 (95% CI: 0.826–0.848), 0.740 (95% CI: 0.727–0.753), and 0.691 (95% CI: 0.677–0.704), respectively.

**Conclusions:** HPI can be used as an aid in the hemodynamic management of patients undergoing liver transplantation. Predictability was the highest in the neohepatic phase and the lowest in the anhepatic phase.

This study was supported by the Korea Medical Device Development Fund grant, funded by the Korean Government (Ministry of Science and ICT, Ministry of Trade Industry and Energy, Ministry of Health & Welfare, and Ministry of Food and Drug Safety) (project number: 202011B23).
Anesthetic Management of a Glycogen Storage Disease Type 1A With Air Embolism During Liver Transplantation: A Case Report

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Introduction: Glycogen storage disease type 1a (GSD-1a) is a rare autosomal recessive inborn error of metabolism caused by deficient activity of G6Pase. Orthotopic liver transplantation (OLT) may be considered in patients with difficult metabolic control despite medical treatments. We present an anesthesiologic approach in a rare patient with GSD-1a who developed venous air embolism (VAE) during OLT.

Case Presentation: OLT was planned a 1-year-old boy diagnosed with GSD-1a. He had poor metabolic control and resistant lactic acidosis. CHILD-score as A and PELD-score as 0. On preoperative evaluation the patient was fasted for 4 hours before surgery. To prevent hypoglycemia, infusion was started with dextrose solution and close blood glucose monitoring was performed. During intraoperative organ dissection, sudden hypotension and a drop in end-tidal CO2 occurred after rupture of the vessel wall due to dilatation of the hepatic vein. VAE was considered and an attempt was made to aspirate air from the central venous catheter. After the new air supply was blocked by the surgical team, the patient was ventilated with 100 % oxygen. However, the patient was immediately placed in Trendelenburg and left lateral positions, and vasopressor support was started. With all these interventions, hemodynamic stabilization was achieved. The patient was transferred to ICU postoperative as intubated with vasopressor support. The patient was extubated according to the weaning criteria following consciousness. His neurological examination was normal, therefore no complication due to VAE was suspected.

Discussion: Glycogen storage diseases occur as a result of enzymatic abnormalities that lead to abnormal concentrations or structures of glycogen. As fasting hypoglycemia is the most important problem of the disease, a short duration of preoperative fasting is recommended for such patients. We offered 4 hours fasting to our patient and started infusion of dextrose solutions. VAE is the condition in which air enters the systemic venous circulation from the operation area or during interventional procedures. Intraoperative VAE in OLT is an important complication. A sudden decrease in end-tidal CO2 in anesthetized patients may appear as the earliest sign of air embolism. Hypoxemia, hypercarbia, hypotension, tachyarrhythmias were seen. In our case, almost all of these findings were seen. After the diagnosis of VAE, early intervention is very important. In our case, we intervened in our patient by following the intervention algorithm for VAE. No complications were observed due to VAE in our patient in the postoperative period.

Conclusion: In conclusion, GSD-1a is a rare disease that can cause serious multisystemic problems, therefore anesthesia management of these patients requires a multidisciplinary approach. Although the frequency of air embolism in OLT surgery is not very high, intraoperative close follow-up and early intervention is important to avoid long term complications.
Belt & Road Organ Donation Capacity Improvement Cooperation Training Project (BROAOD)

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1DTI Foundation, Barcelona, Spain; 2Medical School, University of Barcelona, Barcelona, Spain; 3China Organ Transplantation Development Foundation, Beijing, People’s Republic of China; 4Institute for Hospital Management, Tsinghua University, Beijing, People’s Republic of China.

Background: The lack of awareness and knowledge about organ donation (OD) and transplantation (OT) among health professionals is one of the main reasons contributing to donor shortage. Seeing the need to improve the donation activities in China and Belt and Road countries, China Organ Transplantation Development Foundation and Donation (COTDF) and Transplant Institute (DTI) Foundation jointly initiated the Belt and Road Organ Donation Capacity Improvement Cooperation Training Project to provide intensive training in OD and OT to health professionals from these regions.

Methods: The program used an interactive and dynamic online modality consisting of round table discussion, presentation of clinical cases, gaming, and workshop interaction. The bilingual training (Chinese and English) adopted the best practices in OT and OD and was delivered by international experts. A questionnaire to evaluate changes in perception, confidence, and capability towards essential components of organ donation was administered pre-and post-course.

Results: Three editions of the 3-day course were conducted in May, August, and December of 2021. A total of 182 participants were trained, of which 23% (n=42) were international participants from the B & R countries. The participants consist of majority intensive care doctors and other health professionals involved in OT and OD such as donor coordinators, emergency physicians, and nephrologists from more than 60 different hospitals. Seventy-four matched pairs of responses from the pre-and post-course survey were available for analysis. Whilst 16% of the participants showed positive change in their perception towards organ donation, majority (77%) expressed that their perception remained unchanged. Increased confidence was observed among the participants in effective donor maintenance (19/74; 26%), communication with coordinator (17/74; 23%), initial family communication (16/74; 22%). There was 24% (18/74) showed decreased confidence in detection of potential donor. Large proportion (55 – 78%) of the participants stated no changes of confidence in these areas. Nearly all the participants showed above average improvement of capability in various processes of organ donation.

Conclusion: This program improved the capability of the participants to perform donation activities. Continuous and in-depth training with more simulations is needed to further enhance confidence of the health care professionals especially in donor detection. The course served as a platform for the participants to exchange opinions and differences in practices with international experts. This international cooperation initiative promoted by the COTDF and DTI Foundation is an excellent example of leading international engagement and supporting the global community to reach self-sufficiency in OD and OT.

Impacts on NHS Renal Transplant Educational Service Delivery During the COVID-19 Global Pandemic

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Introduction: During the current covid-19 global health pandemic the delivery existing face-to-face patient healthcare education in extremely vulnerable patients has posed several challenges. Adaptations to the delivery of healthcare provisions have been vital to prevent unnecessary exposure of patients to risky hospital environments. Covid-19 created multiple constraints on patient care. This included our clinical teams own ability to interact directly with potential renal transplant recipients in the pre-existing conventional manner. Pre covid-19 pandemic, the renal transplant unit at Leicester General Hospital established comprehensive patient information sessions which were patient facing, forming the initial transplant recipient assessment process and the introduction for potential live kidney donors. However during the pandemic information sessions have unfortunately been postponed until the patient attends the transplant assessment clinic appointment with the surgeon, or when the potential live donor attends the hospital to be assessed by our live donor coordinator. To adhere to social distancing guidelines we developed and initiated a pilot programme for such patient’s which involved a structured virtual process delivered from an online platform.

Methods: A Single centre study which involved patients attending in November 2020 accessing Microsoft Teams, listening to the live presentation from the lead transplant consultant and coordinators. The electronic equipment that patients required access to was either a laptop/computer or a smart mobile. The session allowed for live interaction and patient participation.

Results: Initial pilot: 11 patients participated in the virtual session, 3 potential donor and recipient pairs. Patients included; either being assessed for suitability for renal transplantation or commencing the live donor work up process. Participants were asked to complete an online feedback survey following completion of the session. 8 questions were formally analysed, 72% answered. Patient outcome data supported the pilot study and patient feedback was favourable for this method.

Conclusion: The pilot suggests that we have safely demonstrated that the delivery of healthcare can effectively be modified to safeguard patients, particularly those classified as extremely vulnerable, thus preventing unnecessary hospital exposure during the covid-19 global health pandemic. The delivery of patient facing care has successfully been adapted without compromising care standards.
P5.03

Teaching the New Medical Specialties: Transplant, the Challenge of Accompanying Scientific Progress From Education

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Introduction: The shortage of organs continues being a sanitary problem, one of the main causes is the lack of knowledge of the health team. The teaching of the "Transplant" subject in the medical career allows to integrate knowledge from different disciplines (medical, ethical, legal and surgical), it promotes reflection on ethical values: dignity, solidarity, accessibility and donation awareness.

Method: In 2007, "Transplant" was incorporated as an optional subject in the medical career during the last year, with a total of 40 hours: 32 theoretical (T) and 8 practical (P). The content (T) covers three units: ethical-legal, medical procurement and transplant. While (P) is completed with an internship in the procurement organism. The evaluation was carried out as a multiple choice exam. Qualified: Very good (VG): 8 or more; Good (G): 6 and 7; Regular (R): 5 and 4; and Bad (B): 3 or less; and a group monograph. The adherence of the students to the subject on an annual basis, the academic performance and the degree of satisfaction of the students were analyzed through a voluntary survey.

Results: 259 pupils (P) were evaluated from 2007 to 2024 (X=18 P per year). The grade of 234 (P) was (MB) and 25 (P) was (B). All of them had good disposition to group work and the compliance with the internship was 100%. The evaluation of the chair carried out by 183 (P) revealed two predominant aspects: 1- Satisfaction with the contents and the quality of the theoretical classes and 2- The incorporation of the importance of donation and the proposal of including the subject as compulsory (30%).

Conclusion: The incorporation of the "Transplant" subject constituted a positive experience as a teaching strategy for the integration of knowledge. It allowed (P) to become aware of the importance of donation and gave them knowledge about a new specialty of medicine.

P5.04

Knowledge About Donation and Transplantation in the Health Team

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Introduction: One of the main causes of the deficit of organs for transplantation is misinformation. A survey carried out by 5th year students of the USAL medical career to health professionals was presented, to evaluate the knowledge about donation and generated proposals to improve the problem.

Method: Closed survey conducted in the field in eight (8) hospitals in CABA and one (1) in BA; The interviewers were 5th year students of the USAL medical career, students of the subject “Organ Transplantation”.

Results: 85 surveys were analyzed, two were discarded because they had been completed by students. The total evaluated: n= 83. Male: 41 (49%); Female: 42 (51%). Profession: Nurses: 9 Doctors: 74 (urgency 45%, clinic 36%, Surgery 5% no record 14%).

Questions and answers:
1. Do you think there is a person in charge of Procurement and Transplantation of organs and tissues/coordinator in your Hospital? Yes 81% - No 19%
2. Would you donate your organs? Yes 88% - No 12%
3. Do you know the National Transplant Law? Yes 58% - No 42%
4. Do you have information about transplants? Very good 29% - A little 64% - Nothing 7%
5. What subject would you like to receive information from? Organ Distribution 55% - Results of transplant 28% Encefalic death 5% - Others 12%
6. Do you know the dignified death law? Yes 59% - No 41%
7. Do you know the Protocol for Limitation of therapeutic effort? Yes 64% - No 31% - Does not know 5%
8. Do you start a asystole donation program? Yes 59% - No 36% - Do not know 5%
9. Do you know the donation rate? Correct 36% - Incorrect 38% - Does not know 26%
10. Do you know about the waiting list? Correct 50% - Incorrect 34% - Do not know 16%

Conclusions: Health personnel, mostly doctors, are unaware of organ donation, it is aggravated because hospitals are constituted in the natural environment to inform the general public. The need to find a stable link between the medical community and society is imminent, in order to improve communication with the family and improve the number of donors.

Proposal: Education is the main strategy to improve the donation problem. It should be included in the undergraduate and graduate medicine curricula to increase knowledge on the subject and encourage an altruistic attitude such as giving life to another person. Initial education should also include this topic, to raise awareness about donation in the community.
Development of a Multidisciplinary Protocol for Thoracic Organ Donation Process

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Introduction: In Brazil, transplants of solid thoracic organs are less frequent than those of solid organs (kidney organs) is the beginning of a trail of increase in survival and the quality of life of transplant patients, the indication for transplants and the demand for this therapy have grown significantly in the last two decades. However, although the demand and effectiveness of transplants has increased, the lack of organs remains one of the greatest barriers for transplant teams in all countries, as the demand is increasing in relation to the realization of donations, thus increasing the lists waiting. Even with the existence of some protocols for the maintenance of the potential donor, we can observe that the use of organs for transplantation remains reduced in Brazil.

Objectives: To develop a systematic multidisciplinary protocol aimed at the process of donating thoracic organs to the Intra-Hospital Transplant Commission, based on a bibliographic survey of a synthesis of evidence in the specialized scientific literature to assist in the construction of the care protocol.

Methods: Systematic review of the specialized literature to develop a systematic protocol of specific care for chest uptake; construction of a questionnaire based on the scientific evidence researched in the specialized literature, and subsequent technical review of such evidence, carried out by a committee of experts.

Results: Following the selection criteria available in the systematic literature review, twelve (12) studies for the extraction of scientific evidence were listed, all available in English. In all, twenty-one (21) scientific evidences were collected from their total sum. The expert committee was composed of seventeen (17) members, who had access to the questionnaire. The categorization of respondent subjects was as follows: nine (9) doctors, seven (7) nurses and one (1) physiotherapist. The set of evidence shown here can contribute to improving the outcome, in providing reliable scientific information and in a broader field of engagement of the multidisciplinary team in this process. Three (3) domains were designed, and from these the protocol presented here was built.

Conclusion: The study developed the domains of the thoracic organ donation process, and proposed actions that can be carried out by the multidisciplinary health team in the various scenarios existing in Brazilian cities. The review used as a scientific basis systematized new scientific evidence for the academic and/ or care community. Finally, this Multidisciplinary Protocol for Donating Thoracic Organs is the beginning of a trail of knowledge that aims to reduce waiting time and bring more quality of life to the 277 heart transplant candidates and the 195 lung transplant candidates who exist in the country in 2021.

Keywords: organ donation; evidence-based practice; systematic review.

Health Professional Education

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Background & Aim: Currently, we have two main transplantation hospitals and three donor hospitals in Mongolia. Due to growing demand for transplantation and continuous rise on waiting list requires higher knowledge and proper attitude toward organ donation among healthcare staff in Mongolia. We conducted surveys among five subspeciality state hospitals in November 2018. Donor law was revised and enforced since February 2018.

Purpose: Since January 2020 Covid -19 pandemy, most training activities completely stopped. Therefore, we aimed to provide management updates for our healthcare staff and senior medical students.

Material and Method: Power point presentation lecture based classroom education will cover the basic information about organ transplantation, donor card, brain death donor determination, donation and Istanbul Declaration. The our target 5 and 6 th year medical students will given one hour lesson with a companying brochure about the donor legislations, transplantation program, data, benefits of the organ and tissue donation. Case discussion with a companying brochure about the donor legislations, transplantation program, data, benefits of the organ and tissue donation. Case discussion will be our main training method for medical staff at transplant and donor hospitals. Hands on training will be organized on new donor hospitals.

Findings: Brain deceased donor determination team members from main donor hospitals will be our main training method for medical staff at transplant and donor hospitals. Foreign consultants will share their extensive experience with our pancreas, heart transplant team doctors and tendon, skin graft and cornea team doctors.

Conclusion: In order to expand our deceased donor pool and improve public knowledge and attitude toward organ donation in Mongolia, we need to train doctors, nurses and other healthcare staff more frequently. As of March 2022, we have 55600 healthcare staff and more than 15000 medical students. They can provide the accurate information to their family members, friends and communities as our main public education resources. Also, it will help to strength our transplant team work and provide positive impact on newly established other transplant program development and progress.
Impact of the Liver Transplant Pharmacy (LTP) At the Center For Liver Transplant and Hepatobiliary Surgery (CLTHPS) in Educating Our Transplanted Patients in Costa Rica. A Comparison of Benefits to a Traditional Model Pharmacy

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Introduction: The social security in Costa Rica has institutional pharmacies with traditional models supporting transplant programs (not fully dedicated to this matter). The LTP at the CLTHPS represents a unique and innovative model of care for transplant patients. The LTP has specialized workers who dedicate all their time to attend the liver transplanted population, those who are in the waiting list and also, the patients who have had any hepatobiliary surgery, encompassing a comprehensive attention from the admission until hospital discharge, as well as outpatients. Part of our success has been an active education program and a personalized pharmacy for the particular needs of each patient. The LTP guarantees an open and permanent communication between the patient and the pharmacist, who has a permanent position in the LTP, allowing her to know globally every patient, their medications, lifestyles, nutritional issues, etc. In this way, the pharmacist identifies the needs of each patient, and works hand in hand with each patient in a multi-step approach of education, including: medicament education and dispensations, resolution of doubts about dosage, interactions and side effects and informative material, etc.

Methods: We want to compare the impact of our educational program at the LTP with the counterpart made in a traditional model pharmacy (TMP) for a whole year. We have our monthly indicators in which we register all the production we made, including the educational part, as well as the amount of medication refunded by non-withdrawal. All institutional pharmacies measure the monthly production and that data is accessible, for further comparison of information between our LTP and a TMP. The closer TMP to the LTP is the Hospital Mexico’s Pharmacy, so we’ll work with its yearly production.

Results: What we expect to find is that the LTP has a stronger impact in educative benefit for our patients, according to the quantity of attended patients, based in the quantity of non-withdrawal prescriptions and reduction of misinformation using the prescribed medication.

Conclusions: Our LTP, with a defined attention program, not only helps our patients with a personalized education to have a better comprehension of their medication, but also makes the non-withdrawal prescriptions to maintain in low rates.

Cognitive Profile and Educational Trajectory in Adolescents And Young Adults With Liver Transplants at the Garrahan Pediatrics Hospital

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Introduction: Chronic liver disease and the transplantation process can affect cognitive function due to multiple risk factors (medication in early stages of development, prolonged hospitalization, associated complications, etc). Neurocognitive assessment allows an analysis of the brain-behavior relationship, which is useful to detect and objectify nervous system dysfunctions. Previous studies describe borderline intellectual functioning in psychometric techniques that assess general IQ in pediatric liver transplant patients; these results demonstrate the need for neurocognitive stimulation and scaffolding to ensure access to learning. Currently, the cognitive profile and educational trajectory in this population is unknown.

Material and methods: Descriptive, prospective, observational study. Forty-five liver transplant patients older than 17 years old seen during December 2021 - March 2022 were included. Assessment instruments: Schooling-oriented interview, Stanford Binet Intelligence Scale IV, D2 attentional test.

Objectives: To describe and analyze the cognitive profile and educational trajectory in the adolescent and young adult liver transplant population.

Results: With a mean age of 18 years old, 6.7% had dropped out of school and 22.2% had completed secondary education. Ninety-one percent were receiving formal education, with 60% having discontinuous schooling trajectories due to high repetition rates. Sixty percent were in regular schooling and 6.3% in special schools; 4.4% had an inclusion teacher. With reference to the cognitive evaluation, in 55% of the cases a representative mean of the total IQ could not be obtained, given the discrepancy between the cognitive functions (more than 1.5 deviations of differences between scales). The analysis of this discrepancy results from the significant compromise found in the area of verbal reasoning in 69%. In the remaining sample, the mean IQ found was 69, corresponding to mild levels of compromise. Regarding tasks of attentional control regulation, execution of an action plan, divided attention and cognitive flexibility, 78% obtained levels of compromise, 55% presented indicators associated with distractibility and 48% showed impulsivity in the task. Working memory presented borderline levels in 41.9% with greater strengths in visual input.

Conclusions: The results show discrepant cognitive profiles with greater affectation of verbal reasoning. Executive functions showed levels of compromise, being visual working memory the most preserved aspect. Given the interrupted educational trajectories, it becomes necessary to objectify the importance of an early evaluation of development and learning, in order to guarantee pedagogical continuity and access to the pertinent therapeutic and school support.
Education in the Donation-Transplant Process in Undergraduate Medical Training

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Introduction: Training in transplants of organs, tissues and cells, as a therapeutic modality of multiple pathologies, is essential in undergraduate education. The future doctor cannot ignore the general aspects of the donation-transplant process, from different perspectives. On the other hand, the procurement and transplantation process provide a pedagogical scenario for the integration of medical knowledge, given its interdisciplinary nature, which covers all the subjects of the Medical Career. The medical aspects, typical of the theme, are associated with the ethical, legal, religious and philosophical, giving a holistic view of the process. We present a teaching model of the donation-transplant process with 15 years of experience.

Materials and Methods: The subject Organ, Tissue and Cell Transplants began its activities in 2008. It is an elective, annual subject, included in the last year of the Medical Career. Since its inception, it has established a continuous teaching methodology with a global approach to the donation and transplantation process. Its development is presented in 27 modules that are grouped into 2 themes: Donation and transplantation. The activities derived from them develop the modalities of seminars, workshops, practical activities in the room and critical units, specialized external office, operating room and a final integrative workshop. In this way, the teaching objectives of addressing the cognitive, psychomotor and affective areas with a concept of integration of knowledge in a vertical and transversal way are met. The continuous evaluation is carried out in each face-to-face activity, 1 partial evaluation on donation, 1 partial evaluation on transplantation and a final evaluation.

Results: During the 15 years and until the moment of the presentation, 1057 students have registered for the subject, 80.6% (852) completed the requirements of approval of the course, presented to the final evaluation, 79.9% of the students (681), 96.4% (654) of the students passed the final assessment. The average final grade calculated was equal to 6.53 ± 2.9 points, out of a total of 10; 205 students (19.4%) still need to comply with the final evaluative instance. At the end of the subject some students have joined the basic and translational research team, others have developed their Doctoral Thesis in the subject of Transplantation and others integrate transplant teams from our country.

Discussion and Conclusion: The subject allows the advanced student in medicine to be educated in a subject little explored in other pedagogical instances, provides a framework for the integration of all the subjects of the career and instructs about the ethical and legal responsibilities to future professionals. In the available literature there are different training modalities, but none resembles the model presented. Finally, it is concluded that, during these fifteen years, the pedagogical expectations and in the training of human resources have been exceeded.

Education of Medical Students on Organ Donation and Transplantation

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Introduction: We have been teaching transplantology since 2017 within the 72-hour course for sixth-year students. We analyze this experience in order to increase activities and manage inequalities in organs transplantation.

Methods: The educational program consists of seven topics: 1) selection and preparation of transplant recipients; 2) artificial organs; 3) organ donation; 4) technical aspects of organs transplantation; 5) immunosuppression after organs transplantation; 6) postoperative management of transplant recipients; 7) infectious diseases during organs transplantation. Part of the classes was online with correction of the teaching design and technical support because of the COVID-19 pandemic. There have been evaluated the role of the knowledge gained at the previous stages of educational process and the possibility of solving key regional transplant problems based on training.

Results: From September 2017 to February 2022, 1400 students have had specific training on transplantation. All of them show a positive attitude towards proposed program. Study of transplantology allow summarizing the data from the wide list of disciplines and it shows how great their practical significance is. The initial level of knowledge presupposes the use of previously studied theoretical and clinical material, including questions of anatomy, physiology, diagnostics and treatment of diseases of the kidneys, liver, heart, lungs, pancreas and brain. Students should, but not always can evaluate properly the functions of vital organs at various stages of their diseases. Especially this concerns the brain death as a criterion of human death and the criterion for stopping resuscitation. Also it was found that the main attention at the previous stages of students' training is paid to conservative therapy of end-stage organ failure and this requires appropriate retraining of other teachers in order to form a positive opinion about the modern possibilities of transplant surgery. "Quality of life" as a criterion of choice in the treatment of end-stage organ failure should also be considered at all stages of education. The purposeful and active focus of the new generation of future doctors on the issues of transplantation in the next 5-10 years will allow eliminating the key regional transplant problems, such as late referral of patients, organs shortage and imperfect logistics.

Conclusion: Today's medical students will be tomorrow's doctors and implementation of specific programs on transplantation should be considered as a reasonable step. Interdisciplinary integration as a tool that allows carrying out the necessary activities in organs transplantation requires improving the cause-effect relationships between the knowledge acquired at different stages of education. In the future, this will provide the necessary conditions for the widespread introduction of organs transplantation within the framework of public confidence based on common values and ideas.
Organ Donation for Pre-medical Students

Developing a Standardized Education Program on Deceased Organ Donation for Pre-medical Students

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Introduction: It is necessary to deliver essential knowledge on deceased organ donation to medical and premedical students who will play an important role in the field of deceased organ donation in the future. To increase awareness and knowledge on deceased organ donation through a systemic education, we developed educational content and contents delivery pathways for pre-medical and medical students and evaluated its educational effect.

Method: On- and off-line self-learning aids materials on 7 topics on deceased organ donation were generated and posted on the Vitallink Academy YouTube site. Pre- and post-education questionnaires (32 and 15 questions, respectively) were developed using a web-based survey platform. The survey consisted of items related to awareness, knowledge, and attitude to deceased organ donation. These surveys were conducted before and immediately after the education process. The education was proceeded according to the following 3 steps (1) Group study sessions on selected topics, (2) Poster submission on the given topic by each group and excellent poster selection by the organizing committee, and (3) Excellent poster presentation and Q&A.

Results: A total of 141 students in the first grade at the premedical course at the Seoul National University College of Medicine participated in this program. Even though 96% of students had heard about deceased organ-tissue donation, only 2.1% said that they know about it well. 33.3% of students showed interest in the deceased organ-tissue donation-related issues, 24.2% agreed that anyone who was diagnosed with brain death should donate. Students will agree to donate if their family member had registered (88.9%) or if the person had expressed wishes to donate while alive (63.6%). Most students (83.8%) said that courtesy for deceased donors is necessary or very necessary through funeral support services (35.4%), and the establishment of the memorial park or memorable monument (22.2%). Interest in deceased organ-tissue donation-related issues increased from 33.3% to 84.9% by education (P<0.001). The proportion of students with a positive attitude toward organ-tissue donation was increased from 74.7% to 97.7% (P<0.001). Their attitude toward deceased donation evaluated by expressing willingness to organ-tissue donation also increased from 76.8% to 96.5% (P<0.001). The proportion of accepting brain death as a death increased from 61.6% to 89.5% (P<0.001). Moreover, 81.4% of students had changed in minds and planned to sign up for brain death organ donation registration.

Conclusion: Among many avenues of improving public awareness in deceased organ and tissue donation, target-specific education could be the best way in increasing family agreement in countries adapting the Opt-in system. Significant improvements were observed in knowledge and awareness which is enough to bring changes in attitude when we applied our newly developed education program to a group of premedical students.

Quality Appraisal of Evidence-Based Guidelines for the Health Education of Solid Organ Transplantation

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Objective To evaluate the evidence-based guidelines for the health education of solid organ transplantation at home and abroad, and analyze the characteristics of each guideline, so as to provide references for the education of transplantation in China.

Methods We conducted a systematic retrieval of the relevant guidelines on health education of solid organ transplantation published or updated since January 2011 until January 2021, in authoritative domestic and foreign guide websites, the website of the professional society of transplantation and Chinese and English databases. We used AGREE II to evaluate the chosen guidelines.

Results A total of 8 relevant evidence-based guidelines at home and abroad were retrieved. The average standardized scores of quality evaluation for the 6 areas were 87.82% for scope and purpose, 75.46% for participants, 66.54% for rigor, 90.16% for clarity, 48.18% for application, and 74.13% for independence. For overall quality, 2 was Grade A and 6 were Grade B.

Conclusion Guidelines for different types of solid organ transplantation were at different levels, the quality of guidelines needed to be improved, and contents needed to be refined. In the future, we can learn from high-quality guidelines and develop local guidelines in China to guide the health education of organ transplantation.
P5.15

Build-up on School Education Program to Nurture the Value of Sharing and Deceased Organ Donation for Youth in Korea

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Introduction: In order to form a social consensus on deceased organ donation, it is necessary not only to promote through events, but also to nurture the value of sharing and understand deceased organ donation by school education.

Methods: Vitallink, an NGO established by medical professionals, has built network with school teachers since 2015 and developed a guidebook and built four-hour class program. The guidebook called ‘The Seed of Hope, the Fruit of Sharing’ is composed of 14 chapters, the first part of which deals with the value of sharing and the latter part consists of understanding of deceased organ donation. In 2019, Vitallink collaborated with teachers to conduct the ‘Sharing & Life-sharing’ classes based on the guidebook and did a brief survey (5 questions) after class in one high-school. During the covid-19, school education had been converted to online, so the education was revised accordingly to four-hour class ‘Respect for Life’, which was composed of loving myself, empathizing and coexisting with others, and practicing sharing. Teachers who developed this program conducted pilot classes in elementary and middle schools. In February 2022, we held the zoom symposium on the four-hour class program for teachers, and then conducted a 7-item questionnaire.

Results: A total of 120 high-school students participated in ‘Sharing & Life-sharing’ classes and 115 students responded the 5-question survey. Only 41 percent students replied they have heard of deceased organ donation to some extent and 69 percent of students answered that they felt need of this education. In February 2022, twenty-five teachers participated in the zoom symposium and sixteen completed the 7-item survey. Most of the participants (87.5%) said that this four-hour of ‘Respect for Life’ class at school were necessary for their students and 81% of teachers said they would be willing to conduct this program at school.

Conclusions: We have experienced positive changes in our lives while developing this Sharing & Life Sharing education program. If this program is established in schools, the culture of deceased organ donation is expected to change positively with time and be put into practice.

P5.16

Learning From the Learning Curve: The Personal Database of an Entry-Level Transplant Surgeon as a Tool to Improve Outcomes

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Background: The transition from a trainee to an independent surgeon is a long and gradual process. We present an example of using of personal cases database as a self-learning, practical tool for a beginning transplant surgeon for improving outcomes.

Methods: Data from a single surgeon post-fellowship initial experience in deceased donor kidney transplants, including donors, recovery and preservation features, recipient demographics and pre-operative characteristics, peri-operative surgical data, and short-term outcomes, has been systematically collected. After the completion of the first 20 cases (Group 1), the data analysis was performed, resulting in subsequent modification of surgical planning and technique. The data from the following 20 cases (Group 2) was analyzed and compared to assess the effect of changes made.

Results: No difference was observed in recipient age, sex, body mass index BMI and calculated peri-operative risk. Kidney donor profile index (KDPI) and cold ischemia time (CIT) were higher in group 2 (37% vs 44% and 15 vs 17 hours, group 1 and 2, respectively). Operative time and warm ischemia time (WIT) improved in group 2 (4 vs 3.3 hours and 39 vs 35 minutes, group 1 and 2, respectively). Blood loss was not different between the groups (100 ml). Group 2 had improved hospital length of stay, total and major complication rates, and re-operation rate (Table). The delayed graft function (DGF) rate was higher in group 2. All patients with DGF had a recovery of graft function and all 40 patients maintained preserved graft function during the median follow-up of 6 months.

Discussion: Based on data analysis from the first 20 transplant cases, modifications were made to the surgical technique, such as exposure and vascular clamps. That led to an observed improvement in perioperative and short-term outcomes in the next 20 cases. The higher rate of DGF can be explained by longer CIT in Group 2. Group 2 had improved hospital length of stay, total and major complication rates, and re-operation rate (Table). The delayed graft function (DGF) rate was higher in group 2. All patients with DGF had a recovery of graft function and all 40 patients maintained preserved graft function during the median follow-up of 6 months.

Outcome (30 days) | Group 1 | Group 2
--- | --- | ---
Median hospital length of stay (days) | 5 (4-8) | 4 (3-5)
Step-down unit length of stay (days) | 2 (1-3) | 2 (1-3)
Total complications rate | 15 (75%) | 10 (50%)
Major (Clavien 3 and above complication rate) | 4 (20%) | 1 (5%)
Re-operation | 2 (10%) | 0 (0%)
Delayed graft function (DGF) rate | 6 (30%) | 8 (40%)
**P6.01**

**Actuarial Perspective on the Immunosuppressive Medication Costs and Coverage for Transplant Recipients in the Argentine’s Public System: 2009-2021**

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**Introduction:** In 2007, a National Post-Transplant Follow-up Program (PNSPT) was created, which is managed by the Special Programs Coordination Unit (UPSP). One of the objectives of this Unit is to provide immunosuppressive drugs to patients with exclusive public coverage and some special programs. The PNSPT program includes stages that involve the purchase of medicines requested by the Ministry of Health (according to the history of consumption and the balance between registrations and withdrawals of the beneficiary); and the collection in Logistics Operators (medical prescription, request for medicines from each jurisdiction, distribution logistics, patient care and stock management). The cost of immunosuppressive drugs is high, highly variable, and poorly understood. Therefore, the objective of this study was to analyze the evolution of the PNSPT program in compliance with the coverage of immunosuppressive drugs.

**Methods:** This is a descriptive study. The data was obtained from INCUCAI’s National Purchasing and Transplant Information System (SINTRA). The different program regulations were reviewed and medication shipments to the provinces registered and systematized. Subsequently, the following were evaluated annually: the number of patients in the program and the formulary; the amount of medicines distributed, the investment in US dollars made according to the prices paid for each medicine according to the purchase order of the last tender (to control the inflationary effect that occurred during the period analyzed).

**Results:** PNSPT coverage has steadily increased from 705 patients (2009) to 4,261 (2021). Investments in medicines increased even more, going from US$1.1 million in 2009 to US$13.1 million in 2021. Thus, the direct increase in the average investment per patient doubled between the periods analyzed (2009: $1,559.9; 2021: $3,010.6). The largest investment was in 2019 and there was a slight decrease in the following 2 years, as a result of changes in the management of the Program, related to the search for efficiency in the use and purchase of medicines.

Throughout the analyzed period, the vademecum included drugs such as Everolimus, Azathioprine, Tacrolimus XL, Meprednisone, Sirolimus, Thymoglobuline, Valganciclovir, Ganciclovir, Basiliximab and Belatacept; Oral sirolimus and eye drops for pre and post corneal transplant treatment.

**Conclusions:** From the creation of the PNSPT, the INCUCAI increased the coverage and the annual investment for transplant patients with exclusive public coverage and for the beneficiaries belonging to the other coverage under the program. The expansion of the vademecum allowed patients under the program in all regions of the country to have full coverage of induction and immunosuppression drugs. Taking into account that the medication favors the patient’s adherence to the treatment, it is probable that the correct execution of the program benefits the patient, increasing the survival of the graft and the patient.

![Annual investment in US$](image)

**P6.02**

**Provisional and Promising Bioethical Conclusions on Uterine Transplantation**

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Partial conclusions of a research still in progress on bioethical aspects of uterus transplantation at the Faculty of Law of the University of Buenos Aires (Argentina):

1. Uterine infertility (congenital or acquired) affects 1 in 500 women of childbearing age.
2. The authors compare TxUt against other types of treatments and possibilities for infertility and state that: a) although adoption is a path to motherhood and fatherhood, it does not solve the reproductive problem of the couple; b) gestation by substitution exhibits controversial points, fundamentally the lack of homogeneous acceptance of it in the different countries (in this respect, the same could also be said of the TxUt) and the eventual commercialization of the practice. In favor of alternative paths, the ethical dilemmas of the TxUt, the health cost and the technical complexity of the procedure are usually emphasized.
3. The counterargument to the alleged commodification highlights the altruistic nature of organ donation in general and is somewhat weak since it is not refuted. However, he points out that the donors (especially when they are related to the recipients) achieve benefits of a psychological nature knowing that they are contributing to the formation of a family or that the hysterecmy represents a positive change in their physical health every time. that, for obvious reasons, they will never suffer from cervical cancer.
4. On the other hand, the risks involved in undergoing a highly complex surgical intervention are often opposed, since there is consensus among the teams that perform TxUt regarding the preference for living donors.
5. There is still a debate about the time between TxUt and embryo transfer. Most teams still opt for a one-year interval. A no minor bioethical issue at this point is represented by the manipulation, discarding and loss of embryos. The majority of the literature agrees that the information we have is still very limited and that more data is needed, which is why long-term follow-up of donors, recipients and newborns is necessary to improve and better understand the procedure, the risks and benefits.
6. With regard to the impact it has, especially on gender issues, it can be seen that this procedure has the potential to exploit vulnerable women. A not minor problem here is to what extent desire can become a source of rights.
7. Finally, among the bioethical limits converge issues such as the costs of the procedure and the eventual impact it could have on the public accounts of the states when faced by the health systems.
P6.03

Traumatic Events and Treatment Non-adherence: A Potential Association?

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Introduction: Organ transplantation requires, as an essential part of the treatment, adherence to immunosuppressive medication. In adolescent patients, treatment non-adherence rates are higher than in adults and, in some cases, may be associated with experiencing traumatic situations. There is little information on how such an event could lead adolescent patients to discontinue their immunosuppressive medication, thus putting the transplanted organ at risk.

Objective: To describe treatment adherence and its association with traumatic events in adolescent kidney transplant patients. To describe patients’ perception of satisfaction with their transplant.

Methods: A semi-directed telephone survey of adolescent kidney transplant patients was carried out. The SMAQ test (Simplified Medication Adherence Questionnaire) and the Davidson Trauma Scale were used.

Results: Thirty-two kidney transplant patients (TXPs) were interviewed, 17 of whom were female. Their average age was 21±1.8 years. Their education level was: completed secondary school in 14 TXPs (43.7%); incomplete secondary school in 9 TXPs (28.12%); incomplete tertiary education in 7 TXPs (21.87%); and incomplete primary school in 2 TXPs (6.24%). Cohabitants were parents for 22 TXPs (68.7%) and partners for 10 TXPs (31.3%). The average length of time after transplantation was 8.41 years (1-16). Thirty-one Ps were transplanted from deceased donors and 1 from a living donor. Non-adherence was found in 28 TXPs (87%) and only 4 TXPs were adherent (12.5%). Nine TXPs (28.12%) were diagnosed with acute rejection, all of whom were non-adherent. Three TXPs (9.37%) experienced traumatic events, all of whom were non-adherent. Of the 28 non-adherent TXPs, only 3 (10.7%) considered traumatic events as a cause. When asked about the transplant perception, 25 TXPs (78.1%) answered that it had improved their quality of life; 5 TXPs (15.62%) stated that they were satisfied with the transplant; and 2 TXPs (6.24%) did not mention any changes. Thirteen (43.3%) of the 30 TXPs who stated an improved quality of life or satisfaction with their transplant answered that stopping dialysis was the most important change they experienced. Thirteen (43.3%) of the 30 TXPs who stated an improved quality of life or satisfaction with their transplant answered that stopping dialysis was the most important change they experienced. Thirteen (43.3%) of the 30 TXPs who stated an improved quality of life or satisfaction with their transplant answered that stopping dialysis was the most important change they experienced.

Conclusion: Non-adherence is still a problem within this population. The incidence of traumatic events, even though it was low, resulted in non-adherence. Non-adherence cannot be accounted for by dissatisfaction with the transplant as most Ps answered positively about it. Stopping the dialysis treatment was the most valued outcome of their transplant.

P6.04

Xenotransplantation and Bioethics

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Method: During the COVID-19 pandemic, an interdisciplinaty Working Group on Bioethics was summoned by the Xenotransplantation Coordination Group, involving physicians, veterinarians, lawyers and social scientists, for determining an ethical framework that took into account responsible care of human beings and animals. The Group conducted biweekly virtual meetings during all 2020 and through the deliberative method reflected on the different scenarios arising from XT, as the rights of patients, access to treatment as a public health policy and care of experimental and supplier animals.

Results: Several issues were identified. In reference to human patients, informed consent should involve not only the patients but also their family and social group, taking into account traceability, protection of privacy, confidentiality and XT-related psychosocial aspects. Public health issues as xenozoonosis and environmental involvement should be considered. Bureaucracy tending to favor the most powerful, conflicts of interest between industry, institutions and the different stakeholders and xenotourism should be avoided. Animals must be respected and protected as sentient beings. For research in animals (gene editing, preclinical studies) to be morally acceptable, selected ethical and scientific requirements must be met: the OMS-IULAS Guiding Principles, application of the 3Rs, acceptable risk-benefit balance, best welfare for the animal throughout its life, duly trained researchers, honesty and scientific rigor and approval and supervision of an Institutional Animal Care and Use Committee; special consideration must be taken when using non human primates. As for potential supplier pigs, the conditions under which they are to be raised and kept must be established (free of specific pathogens, strict standards of good veterinary practice, maximum care of their well-being). Surgeries for the removal of organs must be performed according to the best current veterinary practice, and when possible they will be without recovery.

Conclusion: XT constitutes a milestone in the “scientific revolution” of the 21st century, as was recently demonstrated by the first genetically modified pig heart transplanted into a human patient. New challenges for bioethics that involve issues ranging from public health scenarios, access to these resources, and responsible commitment of the governments in the implementation of health policies should be considered. Animal care must always be involved, as animals are vulnerable beings that depend on the decision of human beings.
P6.05

Depression and Suicide in End Stage Kidney Disease (on Dialysis and Kidney Transplant Recipients): A National-wide Population Study

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Kidney transplantation (KT) improves prognosis not only physically but also psychologically in patients with end stage kidney disease (ESKD). However, there are few comparative studies of psychiatric disorders in patients treated with dialysis and KT in patients with ESKD. 21,809 ESKD patients without depression and insomnia history before starting renal replacement therapy between January 2002- December 2018 were extracted from the Korean National Health Insurance Service database. 17649 patients received dialysis (15537 patients received hemodialysis, 2112 patients received peritoneal dialysis), and 4160 patients received KT. 45.04% (7949) dialysis patients suffer from insomnia whereas 25.72% (1070) KT recipients suffer from insomnia (p<0.001). Compared to KT recipients (8.61%, 358), dialysis patients (22.77%, 4019) were more prescribed anti-depressant medication (p<0.001). Compared KT recipients (0.12%, 5), dialysis patients (0.19%, 33) were more completely suicided (p=0.047).

In multivariate-adjusted analysis, the hazards ratio (HR) of depression was 1.82 (95% confidence interval (CI), 1.62-2.04). In subgroup analysis insomnia patients (HR 2.15, 95% CI 1.86-2.47), living in rural areas (HR 2.04, 95% CI 1.70-2.36), male patients (HR 1.85 95% CI 1.61-2.13), aged under 65 years old patients (HR 1.90 95% CI 1.68-2.14) more prescribed anti-depressant medication.

KT patients have a lower suicide rate than dialysis patients. In addition, KT is effective in reducing the prevalence of depression in patients with ESKD in Korea, especially for insomnia patients, living in rural areas, male patients, and those aged under 65 years old.

P6.06

The Monetary Cost of Delays in Kidney Transplantation in A Public Health Facility in a Developing Country: Kenyan Experience

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Introduction: Kidney transplantation is the preferred choice of treatment for end stage kidney disease (ESKD) as it confers the recipients with better quality of life when compared with other modalities of kidney replacement therapy (KRT). The economic benefits of kidney transplantation are also superior when compared with either dialysis or conservative treatments respectively. In living kidney donations, the pre-transplant evaluation involves sequenced processes aimed at optimizing resources to deliver a kidney transplant within the shortest time. The shortest period of a donor-recipient pair evaluation within our transplant program is three (3)months. Delays in operation for a kidney transplant attracts both direct and indirect costs with the most unavoidable being the direct cost of continued dialysis.

Methods: We set up a study to establish duration of delays in certain processes with the pre-transplant evaluation for donor-recipient pairs from which we could calculate the direct cost of continued hemodialysis (HD) using a twice weekly HD model at approximately 80 USD per session as the amount at which the social insurance reimburses for HD. We considered three (3) months as the optimum and the economic-neutral duration. This was an observational retrospective study conducted at the Kenyatta National Hospital in Kenya over a five-year period between 2010 to 2014. The captured data were analysed using Statistical Package for the Social Science version 20.0. For categorical data, frequencies were calculated as numbers and percentages while for numerical data, the means and standard deviations were calculated when normally distributed while the medians and interquartile ranges were calculated for skewed data.

Results: A total of 99 donor-recipient pairs who had undergone pre-transplant evaluation between 2007 – 2014 and underwent transplantation during the study period were included. The mean age was 37±13 years. Males were 73(73.7%). Sixty two (62.6%) were married and sixty five (65.7%) were in informal self-employment. The median duration taken in the kidney transplant evaluation process was 10 months (IQR 5 – 13). Only six (6) donor-recipient pairs (6.3%) were evaluated within three (3) months period. The remaining 93(93.7%) were evaluated for between four (4) and 84 months. This translated to 891 HD-months within which 7,128 sessions of HD were purchased by the social insurer. At a cost of USD 80 per HD session, this translated to USD 570,240 as being the direct cost required to maintain the patients on HD during the delayed period.

Conclusion: The time taken to go through the pre-transplant evaluation process within our program is long with the cost of maintaining patients on HD presenting an enormous opportunity cost which can be reduced significantly if the pre-evaluation period is shortened to three months.

Keywords: End stage kidney disease, kidney transplantation, Cost, hemodialysis.
Risk Factors for Trauma Death Among Transplant Recipients

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Objective: To identify demographic and morphometric risk factors for trauma death among kidney, liver, and pancreas recipients.

Introduction: Trauma is a leading cause of death in the United States. Individuals with chronic disease, notably cancer, are at increased risk for death due to unintentional injury. This may stem from the psychosocial stress, poor quality of life and physical disability that result from serious illness. Though solid organ transplant has the potential to extend and improve the lives of those with chronic disease, these individuals may remain in a state of suboptimal physical and mental health after surgery that predisposes them to death from trauma.

Methods: A retrospective analysis was performed using UNOS data from 100,705 adults with a history of kidney, liver or pancreas transplant between 2000-2021. Basic patient, donor and transplant characteristics of the two groups (trauma death or all other cause death) were compared via univariate and multivariate statistical analysis. The trauma death group consisted of deceased recipients in the SRTR registry with the diagnosis code TRAUMA: MOTOR VEHICLE ACCIDENT or TRAUMA: OTHER. The risk factors compared include age, sex, ethnicity, wait time, BMI at the time of transplant, history of diabetes, glucocorticoid use, graft failure, as well as donor and transplant characteristics such as organ share type, donor age, sex and ethnicity. Statistical significance was defined by p-value <0.05.

Results: The data included 100,705 transplant recipients in total. The largest proportion of death secondary to trauma was seen in the kidney group (0.8%), followed by liver (0.7%) and then pancreas (0.3%). Male sex was the most significant risk factor for trauma death among kidney and liver recipients (OR=1.67, OR=1.68, respectively). Whites were also at elevated risk for trauma death relative to their non-White counterparts in the kidney and liver groups (OR=1.32, OR=1.31, respectively). In both of organ categories, age conferred a protective effect (OR=0.97 for kidney, OR=0.98 for liver). Unique findings in the kidney cohort include that those with a longer wait time were 0.02% less likely to die from trauma and those with diabetes mellitus were 19% less likely to die from trauma. Whereas kidney recipients who died via trauma were less likely to have experienced graft loss, trauma deaths in the liver group were more common among those with a history of graft loss. The total number of trauma deaths in the pancreas cohort (n=13) was too small to run logistic regression analysis.

Conclusions: Certain demographic characteristics including White race and male sex are associated with increased risk for trauma death among kidney and liver transplant recipients. Advancing age was associated with a decreased risk in these two cohorts. We believe these findings may help identify patients at risk for trauma death and provide opportunities for early intervention to prevent unnecessary loss of life.

Questions About Xenotransplantation in Ethical and Religious Literature

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Transplantation allows you to confidently save the lives of previously doomed patients. The shortage of organ donors not only limits this undeniable achievement, but also raises a series of new ethical questions. We analyzed 102 sources of ethical and religious literature for 2000-2022 in order to isolate the main issues that arise around xenotransplantation. The main ones are the following.

Is it ethical to put humanity at risk by saving one person? The alleged xenotransplantation will lead to the creation of patients in whose bodies animal tissues and organs will live, a kind of xenochimer. A patient with animal organs may be more susceptible to the corresponding infections of these animals. In the body of such a xenochimeric patient, not only the virome inherent in humans will be present, but also in this animal. This transformation can pose a threat to the life of not only him alone, but the whole of humanity. Can we save one patient at the cost of risk to humanity?

Is it ethical to limit the civil rights of a xeno-recipient? This question follows from the previous one. Since the xenochimera poses an increased risk to others due to the possibility of the formation of new infectious threats in his body, it is expected to obtain an irrevocable obligation from this patient before transplantation. Such obligations are called the Ulysses Pact. Undoubtedly, the xeno-recipient will save his life at the cost of his civil rights and freedoms. Is it ethical?

Will xenotransplantation create another reason for discrimination? Apparent humanity will not get rid of the principles of discrimination based on race, nationality, and gender for a long time. Won’t xenotransplantation create a precedent when xenorecipients become the object of discrimination for fear of infection, prejudice, disgust?

Can the creation of xenochimeras be considered an unacceptable interference in the Divine plan from a religious point of view? According to the book of Genesis, animals and man were created on different days of creation and thus refer to different stages of the realization of the Divine plan. Nowhere in the Pentateuch, which postulates the predominance of man in relation to creation, is there any mention of the possibility of creating mixed chimeric organisms of man and animals. To what extent does such intervention in human nature meet the requirements of religious ethics?

Is it ethical to use higher animals for xenotransplantation? If any tools manage to minimize the risk of using monkey organs, the ethical problem will remain – to what extent does a person have a moral right to kill rather complexly organized living creatures with complex nervous activity in order to save the life of their species? We believe that the emerging issues cannot be an obstacle to performing xenotransplantation. However, finding answers to them will increase the understanding and acceptance of this life-saving type of treatment by people of different cultures and beliefs.
Extended Criteria Donor, Cold Ischemia Time and Delayed Graft Functions; Common Ingredients for an Expensive Recipe

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Introduction and objectives: Delayed Graft Functions (DGF) has a relevant impact in Kidney Transplantation (KTx) being associated with suboptimal outcomes and increased healthcare costs. The necessary and increased use of Extended Criteria Donors (ECD) is inevitably linked with more DGF. Cold Ischemia Time (CIT) remains a crucial determinant of DGF. In the UK specific standards of CIT have been established for KTx from Donors after Brain Death (DBD), <18 hours and Donors after Circulatory Death (DCD) <12 hours. In this study we evaluate the incidence and impact of Beyond Standard (BS) CIT in ECD and estimate the cost of DGF in this group of recipients of KTx.

Material and methods: We retrospectively reviewed our database with 218 consecutive KTx and analyzed type of donors, donor characteristics, incidence of DGF and Primary Non Functions (PNF). We also analyzed the CIT and its component defined as Extraction Time (ET) Transport Time (TT) and time from Delivery of the Kidney to Perfusion with Blood called Unit Time (UT). The cost estimate of the impact of DGF was based on the tariff for KTx currently paid by Healthcare Commissioners (HC) in the UK equivalent to £17,000. The cost estimate of DGF was based on available published evidence identifying an increased 10% for hospitalization and further 10% for dialysis sessions >1.

Results: There were 103 (47.2%) KTx from ECD, of whom with a BS CIT were 37/103 (35.9%). Overall, in the ECD group DGF/PNF was observed in 47/103 (45.6%) patients. The incidence of DGF/PNF in ECD KTx with a BS CIT was 22/37 (59.5%) compared with 25/66 (37.9%) in those ECD transplanted Within Standard (WS) CIT (P=0.03). The major component of CIT was UT, representing 70%±15% of the CIT.

There were 115 (52.8%) KTx from SCD, of whom with a BS CIT were 40/115 (34.8%). Overall in the SCD group DGF/PNF was observed in 33/115 (28.7%) patients. The incidence of DGF/PNF is SCD KTx with a BS CIT was 16/40 (40%) compared with 17/75 (22.7%) in those SCD transplanted Within Standard (WS) CIT (P=0.04). The major component of CIT was UT representing 65%±18% of the CIT. Univariate and multivariate analysis of risk factors of DGF is illustrated in table 1.

Cost estimate: In the ECD group, we calculated £151,300 increase of the total cost. The Individual KTx had a mean ±SD cost in BS CIT and WS CIT of £19543.2 ±2173.9 and £18503± 2034 (p=0.01). Similarly, in the SCD group, we calculated £110,500 increase of the total cost. The Individual KTx had a mean ±SD cost in BS CIT and WS CIT of £18692.5 ±2140.6 and £17997.3± 1854.4 (p=0.07). Overall, the total increase of the cost was £261800 and the mean ±SD cost in BS CIT and WS CIT was £19543.2s 2173.9 and £18503 +2034 (s=0.01).

Conclusion: Our series shows that a substantial proportion of KTx have been performed with a BS CIT which certainly influences the incidence of DGF and PNF in KTx especially from ECD and consequently increases the estimate cost. Adequate infrastructure and readiness of all transplant facilities in order to reduce CIT are mandatory for accepting ECD.

<p>| Table 1: Univariate and multivariate analysis for risk factors of delayed graft function |
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P6.09

Extended Criteria Donor, Cold Ischemia Time and Delayed Graft Functions; Common Ingredients for an Expensive Recipe
P7.01

Selecting Candidates for Multi-Visceral Transplantation in Neuroendocrine Tumors (NET) of the Gastrointestinal Tract: A Review of Two Cases

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Introduction: Neuroendocrine tumors (NETs) are rare neoplasms arising neurologic or endocrine tissues. These tumors can be seen in nearly any organ system, though they mostly would be present in the gastrointestinal and respiratory systems. In this study, we report two cases of multi-visceral transplantations (MVT) in NET and discuss our indications for MVT among NET patients.

Methods and Results: Case 1: A 44-year-old lady referred with a complaint of acute abdominal pain and small bowel obstruction symptoms in June 2018. In laparotomy, an obstructive jejunal mass, a huge retroperitoneal lesion involving the mesentery and liver, was found. A partial resection of the jejunal mass and palliative anastomosis of the bowel was performed. Histopathologic examinations revealed a well-differentiated NET [G1 (Ki67<1%)]. The patient underwent MVT. She developed an entero-cutaneous fistula ten days after the surgery which was managed. After which the patient was relatively well till February 2021, when she was admitted with severe watery diarrhea. Severe mucosal ulcerations were seen in endoscopy, and rejection was confirmed through pathologic assessments. The patient died despite our efforts.

Case 2: A 46-year-old man who had been suffering from vague abdominal pain and dyspepsia was referred to our clinic in February 2021. He gave a history of 5 kilograms weight loss in the preceding six months. Computed tomography (CT) showed a large lobulated heterogeneously enhancing mass about 150*90 mm in the pancreas with extension to the liver hilum and involvement of spleen and stomach, and signs of partial portal vein thrombosis. The pathologist reported a well-differentiated NET (G2, Ki67<15%, mitosis 1-2/10 HPF). Exploratory laparotomy, performed in May 2021, showed locally advanced pancreatic NET with celiac encasement and involvement of stomach and colon and portal vein thrombosis with varicose veins and portal hypertension, but no evidence of hepatic metastases.

MVT was performed in June 2021. The grafts, including stomach, duodenum, liver, pancreas, and small bowel, were implanted. One month later, the patient complained of diarrhea, 3rd-grade acute T-cell rejection in a small bowel biopsy was reported. However, the liver biopsy was insignificant. Favorably the patient responded well to the treatment, and after six months, closure of ostomy was performed. The patient is alive and well to this day.

Conclusion: We propose the following criteria for MVTx in NETs: Well-differentiated NETs; absence of progression in the last six months; extensive porto-mesenteric thrombosis; intestinal failure with liver metastases; Both superior mesenteric artery and celiac trunk involvement; absence of extra-abdominal involvement that is confirmed by Ga-68 dotatate scan. We should note that this was a case report and larger series are required to support our conclusion.

P7.02

Parenteral Nutrition Free Survival in Pediatric Patients With Short Bowel Syndrome: Transplantation vs. Serial Transverse Enteroplasty (STEP), a Paired Matched Case-Control Study

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Introduction: Intestinal failure (IF) is a reduction of the intestinal function below the minimum necessary for the absorption of macronutrients, water and electrolytes to sustain life growth and in children, making parenteral nutrition (PN) the primary therapeutic approach. The causes of intestinal failure can be anatomic or functional, being short bowel syndrome (SBS) the most frequent. Currently a comprehensive multidisciplinary management provides different alternatives like medical rehabilitation, surgical rehabilitation or intestinal transplantation (ITX) in order to recover intestinal sufficiency. The indications of the different approaches have been modified over the course of the years, and comparison assessments are lacking.

Objective: To compare the time necessary to achieve PN independency, nutritional outcome, and long-term survival of pediatric patients with IF SBS treated with intestinal transplant (ITX) or STEP at our center.

Materials and methods: Observational, analytical, matched case-control and retrospective study, of a group of patients treated from 2006 to 2022 at our unit. The data was collected through review of the patients’ medical records.

Results: A sample of 22 pediatric patients with SBS was selected; two of them were excluded to lack of follow-up; therefore 20 patients met all the criteria and are analyzed. The mean age of the ITx patients was 12.32 ± 4.8 (p=NS), of which 60% were male; while in the STEP group, mean age was 9.24 ± 2.7; 90% were male. Primary diagnoses are shown in table 1.

ITX restored the intestinal length to a 100%, whilst STEP allowed for a benefit of 53.6 +/- 34.98 cm. ITX patients required less time to achieve freedom from PN survival compared to STEP (p=0.001, Figure 1a), 80% of them sustained it throughout the first year; in the STEP group, only 30% of the patients achieved PN independency during that time. Furthermore, 5 years after the procedures, no significant differences were found regarding freedom from PN survival between groups (p=NS, Figure 1b), ITX patients gained a significant amount of weight after 6 months (p<0.0001); while the same effect was observed in STEP patients after 12 months (p=0.004). At 5 years, PN free survivors both in the ITx group and the STEP group were able to sustain weight, in fact a significant difference was obtained comparing with baseline (p<0.0001) and the first year (p=0.0005).

No significant differences were found between those treated with STEP and ITX patients (p=NS) when analyzing the 5-year actuarial survival.

Conclusion: Although with different indications, ITX and STEP allowed a similar percentage of patients achieving 5 years survival free from PN. The initial higher slope observed in the ITX group, decreases in the long term due to intestinal graft loss. STEP required longer time achieve PN independency. Future studies would allow analyzing the long-term impact of both procedures.
P7.03
Analysis of Immune Cells Draining From the Abdominal Cavity as a Novel Tool to Early Prediction of Clinical Events. Prospective Multicenter Study - INIGMA Follow-up Report

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1Multiorgan Transplant Institute, Nutritional Support Unit, Intestinal Rehabilitation and Transplantation, Favaloro University Hospital, Caba, Argentina; 2Translational Research Laboratory and Immunology associated to Transplantation, IMETTyB- CONICET, Favaloro University, Caba, Argentina; 3Pediatric Surgery Service, La Paz University Hospital, Madrid, Spain; 4Department of Surgery, Institute for Clinical Sciences, University of Gothenburg, Gothenburg, Sweden; 5Department of Abdominal Transplantation Surgery, University Hospital Leuven, Leuven, Belgium; 6Immunology and Pathophysiology Studies Institute, School of Exact Sciences, National University of La Plata, La Plata, Argentina.

Introduction:
International Network for Intestinal Graft Monitoring and Analysis – INIGMA project is a multicenter study started in 2015. The rationale of this work consists in that the abdominal drainage fluid collected after intestinal transplant (ITx) contains immune cells trafficking from the implanted intestine, and changes of immune cell composition, especially increase of neutrophils, correlated with the appearance of future clinical events (rejection, infection, or other events). The main objective of this project is to validate this non-invasive method for predict the development of abdominal complications after the first post-op days, based on the analysis of draining cell composition and their correlation with clinical follow-up. Here, we aimed to present a follow-up of our study.

Material and Methods:
This prospective observational study started in 2008 by Favaloro Foundation University Hospital, Argentina and turned into a multicenter study involving the University of Gothenburg, Sweden; University of Leuven, Belgium and La Paz University Hospital, Spain from 2015 to 2022. The cell composition of the abdominal draining fluid and blood collected during the first post-op days was analyzed by differential cell counter and was correlated with the clinical outcome.

Results:
A total of 38 patients (pts) with complete biochemical and clinical information were enrolled by 3 of the 4 centers (Table 1). Blood samples showed a predominance of neutrophils and marked leukopenia, independently of the age, immunosuppressive protocol used, and clinical event reported. Whereas draining cell composition showed neutrophilic predominance when patients suffered intra-abdominal clinical complications that change to a leukocyte prevalence when the clinical event resolved. When a new shift to a neutrophil dominant content is observed in the drainage, it anticipates the development of a clinical event in the peritoneal cavity (26/38 pts). Table 2 summarizes the association between neutrophils and clinical events. Sensitivity=92.9%; Specificity=80%; PPV=92.9%, NPV=80%.

Conclusion: our preliminary results suggest that abdominal clinical events can be early predicted after ITx by analyzing the changes in the drainage cell composition, particularly when a shift to a neutrophilic dominance is registered. Thus, cell counts from the drainage should be included as part of the daily evaluation of pts receiving an ITx. This analysis provides further support to use this non-invasive approach to monitor the grafts and the transplanted pts providing easily information for clinical management decisions. A larger pts cohort should be required to validate this methodology.
<table>
<thead>
<tr>
<th>Patient</th>
<th>Group</th>
<th>Neutrophils presence (days post-Tx)</th>
<th>Post-Tx day of event</th>
<th>Clinical event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.7</td>
<td>Rejection 6</td>
<td>7; 10; 14</td>
<td>Mild rejection</td>
<td></td>
</tr>
<tr>
<td>1.8</td>
<td>Rejection 9</td>
<td>11; 13; 17; 23</td>
<td>Mild rejection</td>
<td></td>
</tr>
<tr>
<td>1.9</td>
<td>Rejection 4</td>
<td>5</td>
<td>Isolated jejunal resection</td>
<td></td>
</tr>
<tr>
<td>1.10</td>
<td>Infection 9</td>
<td>10</td>
<td>Peritonsil, Enterococcus faecalis</td>
<td></td>
</tr>
<tr>
<td>1.11</td>
<td>Infection 8; 10</td>
<td>8</td>
<td>Abdominal collection, Klebsiella pneumoniae</td>
<td></td>
</tr>
<tr>
<td>1.12</td>
<td>Infection 5; 9</td>
<td>7</td>
<td>Peripancreatic abscess, Enterococcus faecalis</td>
<td></td>
</tr>
<tr>
<td>1.18</td>
<td>Infection 4; 6; 9; 12; 15; 17; 19;</td>
<td>7; 11; 15; 19</td>
<td>Re operation (Dehiscence sutures colonic stump); Mild rejection; Severe rejection; Surgical wound infection E. coli, E. cloacae, E. faecium infection Mesogastric abscess Candida albicans; Fever; Drainage abscess Abdominal collection, Candida albicans</td>
<td></td>
</tr>
<tr>
<td>2.1</td>
<td>Infection 1; 4; 14</td>
<td>2; 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3</td>
<td>Infection 3; 5</td>
<td>3; 7; 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.9</td>
<td>Infection 3; 4</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.18</td>
<td>Infection 1; 2</td>
<td>1; 8</td>
<td>Subhepatic collection, K. pneumoniae; E. coli, P. aeruginosa – C. amylancicus</td>
<td></td>
</tr>
<tr>
<td>2.19</td>
<td>Infection 5</td>
<td>5; 6</td>
<td>Subhepatic collection, P. aeruginosa, C. amylancicus</td>
<td></td>
</tr>
<tr>
<td>2.20</td>
<td>Infection 2</td>
<td>3; 7</td>
<td>Periparadic collection, Candida sp</td>
<td></td>
</tr>
<tr>
<td>2.22</td>
<td>Infection 1; 4</td>
<td>6</td>
<td>Periparadic collection</td>
<td></td>
</tr>
<tr>
<td>2.23</td>
<td>Infection 4; 8; 11; 25</td>
<td>5; 8; 11-36</td>
<td>Several collections, Candida sp Two re operation for gastric perforation</td>
<td></td>
</tr>
<tr>
<td>2.25</td>
<td>Infection 1; 5</td>
<td>3; 4</td>
<td>Collection and intestinal perforation, C. albicans, C. glabrata, C. freundi</td>
<td></td>
</tr>
<tr>
<td>1.13</td>
<td>Others 4; 12; 10</td>
<td>10</td>
<td>Pancreatitis, Hematoma</td>
<td></td>
</tr>
<tr>
<td>1.14</td>
<td>Others 5; 8; 9</td>
<td>11</td>
<td>Chylous ascites</td>
<td></td>
</tr>
<tr>
<td>1.15</td>
<td>Others 5</td>
<td>8</td>
<td>Uncharacterized diarrhea/ fever</td>
<td></td>
</tr>
<tr>
<td>1.16</td>
<td>Others 7; 9; 12</td>
<td>12</td>
<td>Eosinophilic gastroenteritis</td>
<td></td>
</tr>
<tr>
<td>1.17</td>
<td>Others 6; 8; 10</td>
<td>Unclear</td>
<td>Hematoma abdominal wall</td>
<td></td>
</tr>
<tr>
<td>1.19</td>
<td>Others 8; 9; 10</td>
<td>8</td>
<td>Uncharacterized fever</td>
<td></td>
</tr>
<tr>
<td>1.20</td>
<td>Others 7; 9; 12</td>
<td>14</td>
<td>Chylous ascites</td>
<td></td>
</tr>
<tr>
<td>2.2</td>
<td>Others 5</td>
<td>5</td>
<td>Bleeding from the gastric anastomosis</td>
<td></td>
</tr>
<tr>
<td>2.21</td>
<td>Others 2; 11</td>
<td>2; 15</td>
<td>Postresection bleeding, Re-operation delayed abdominal closure and removal of the transplanted Id Re-operation for delayed abdominal closure</td>
<td></td>
</tr>
<tr>
<td>2.24</td>
<td>Others 3</td>
<td>5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Episodes of infection and post-Tx clinical event are reported for each patient. The table includes patients with neutrophils in their clinical events, and the post-Tx day of event indicates when the neutrophils appeared. The clinical event column provides details of the specific infections or complications encountered. The groupings and presence indicate the nature of the neutrophilic events.
Case description: A 52 year old man with two month abdominal pain and distension led to Budd-Chiari syndrome diagnosis in November 2018, in other institution. A left hepatic vein angioplasty was done, with dalteparin treatment. After the second dose he showed abdominal rash. Warfarin treatment was used for 5 days without proper coagulation control. A new dalteparin dose induced an anaphylactic reaction with ICU admission. Several weeks later, with the diagnosis of splanchic veins thrombosis, a thrombectomy and portacaval shunt was performed. Shunt thrombosed at second postoperative day. JAK2-positive polycythemia vera was diagnosed and treated with hydroxyurea to keep a hematocrit <45%, and the patient was anticoagulated with fondaparinux. He had a 3 month postoperative stay due to complications. Ascitis developed in 2020, with repeated paracentesis, and a right inguinal hernia. Esophageal varices were treated with elastic bands ligation. The patient retired and moved to other country, and shortly after he was referred to our hospital. CT and MRI showed liver cirrosis with regenerative nodules, portal vein thrombosis and cavernous transformation, with a thrombosed portacaval shunt., and splenic and SMV thrombosis. Sodium heparin tolerance test was decided to rule out problems derived from donor hep- annization, and done at the ICU, without adverse effects. He was listed for multivisceral transplantation on December 2020. Oral anticoagulation with acenocumarol was instituted. A multivisceral transplant was performed on July 2021. Due to anticoagulation (PT 28%), portal hypertension and adhesions and intense fibrosis from previous surgery, massive transfusion was needed: 60 RBC units, 45 FFP units, 5 platelet pools, 8 g fibrinogen, 2000 U Beriplex. Aortic conduit to recipient aorta. A side to side caval suture was performed due to the Budd-Chiari syndrome. Gastric anastomosis with preservation of half the stomach in both recipient and graft. Right colon of the graft to transverse colon in the recipient. Ten days after the transplant he had a reoperation due to spontaneous punctiform perforation at mid-jejenum. Two months after the transplant the liver profile deteriorated due to biliary sludge, and a biliary stent was inserted. Discharged after three months and a half.

Conclusion: Multivisceral transplantation may be a good indication in patients with diffuse portomesenteric thrombosis with procoagulant disorders and challenging anticoagulation treatments.
Endovascular Thrombectomy in a Chronic Upper Cava Syndrome Due to Long Term Home Parenteral Nutrition. New Hope to Extend Life Support

Camila A Cáceres1, Marcelo Dándolo1, Osvaldo Sánchez2, Jimena Alaini3, Ricardo Trucco4, Mariana Ortega4, Héctor Solar1, Gabriel Gondolesi1, Oscar Gural Romero1.
1Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina.

Introduction: Chronic Intestinal Pseudo Obstruction (CIPO) refers to a heterogeneous group of disorders characterized by symptoms of intestinal obstruction, without evidence of mechanical lesion and is a cause of chronic intestinal failure. Loss of vascular accesses by thrombosis has become the current main indication for intestinal transplant.

Materials and Methods: A 28-year-old female patient with a history of myopathic CIPO received Home Parenteral Nutrition (HPN) for 25 years, developing central venous accesses thrombosis. As a consequence of a chronic upper cava syndrome with occlusion of the right jugular and subclavian-axillary vein, an invalidating headache and inability to maintain dorsal decubitus due to retroocular pain evolves overtime, but worsen with HPN infusion, limiting the volume and calories provided. A multidisciplinary case discussion concluded that although chronic, an endovascular thrombectomy should be attempted to improve quality of life and to satisfy nutritional needs.

Results: A vascular computer tomography (CT) scan with 3D reconstruction and a digital venography were performed showing complete occlusion of the right jugular, axillary and subclavian (where a picc-line was placed as last access) veins and a partial occlusion of the proximal superior vena cava (SVC) and occlusion of the right iliac vein. An angioplasty trough the right humeral, axillary, innominate trunk axis and superior vena cava using 6 & 9mm balloons was performed. Balloon dilatation of multiple venous strictures was done, followed by placement of two stents, one into the right subclavian vein and SVC, and the other into left subclavian vein, with restitution of venous blood flow. Anticoagulation with Rivaroxaban and Clopidrogel was started. On the 5th postoperative day a new onset of acute pain, paresthesia were reported, followed by edema in the right upper limb. A Doppler ultrasound was positive for an acute thrombosis, confirmed by CT scan. A new phlebography and mechanical thrombectomy using the ASPIREX device followed by a new angioplasty of a partial distal stenosis was done. A new stent implantation into humeral, axillary, and subclavian veins was performed. Outcome was favorable with complete resolution of the symptoms; being discharged on day 6. The patient currently is asymptomatic, receiving HPN without complications.

Conclusion: This case is an example of the management of deep venous thrombosis secondary to the chronic use of HPN. A comprehensive multidisciplinary approach is mandatory due to its complexity, requiring to be performed by trained and expert interventionists, to successfully provide new alternatives to extend the possibility for their life support or avoid contraindications to transplant. Peripheral venous hemodynamic is not a common procedure however, is the cornerstone to treat this complication achieving in many cases the recovery of venous blood flow delaying the need of intestinal transplantation.

Thyroid Infection Caused by Invasive Aspergillosis in Solid Organ Transplantation: A Case Report

Hector Solar1, Mariana Ortega1, Mariana Doeyo1, Elizabeth Madsen1, Claudia Nagel1, Gabriel Gondolesi1.
1Hospital Universitario Fundación Favaloro, Buenos Aires, Argentina.

Introduction: Aspergillosis is a frequent fungal infection among immunocompromised patients, with an incidence between 0.1 to 11.6% in solid organ transplant recipients. Intestinal transplant patients are at the higher risk of infection; being lungs and central nervous system the main affected organs. Thyroid infection is an unusual extra pulmonary presentation secondary to a disseminated invasive aspergillosis.

Materials and Methods: We aim to report a case of a thyroid infection secondary to an invasive aspergillosis in an intestinal transplant recipient.

Results: A 29-year-old male, with history of chronic renal failure due to nephronophthisis in peritoneal dialysis since 2006, developed Cocoon syndrome. In 2014 a laparotomy was performed due to intestinal perforation and peritonitis. A total enterectomy, subtotal colectomy and cholecystectomy was carried out. Post-surgical anatomy was type 1 with 10 cm of jejunum left. Patient was discharged on home parenteral nutrition. Intestinal Failure associated Liver Disease was diagnosed by liver biopsy (Metavir 3). In 2018 an intestinal, liver and renal transplant was performed. A severe exfoliative cell rejection resistant to the medical treatment of the intestinal graft was developed, so enterectomy of the intestinal graft was performed. The patient evolved with fever, and a positive chest CT scan showing bilateral nodular opacities. Transbronchial biopsy was performed and the presence of Aspergillus nidulans was informed. Patient was started on Liposomal Amphotericin and Voriconazol, four months later Voriconazol was discontinued due to elevation of the liver function tests and completed six months on Amphotericin. The new CT scan at the end of treatment, showed absence of pulmonary infiltrates. But, 1 month later, he developed an indurated, erythematous, mobile, painful on palpation central cervical tumor of approximately 3x2cm, without cervical adenomegalies. A neck CT scan confirmed a thyroid nodule (Fig 1-2), requiring a right hemithyroidectomy. The definitive diagnosis was thyroid Aspergillosis, requiring post-surgical treatment with intravenous izovuconazol and caspofungin. Two months after the diagnosis the patient died due disseminated aspergillosis.

Conclusion: Thyroid aspergillosis disease remains infrequently reported but if occurs, it has a mortality rate superior to 60%. A high clinical suspicion among those high-risk patients should lead to careful examination since most patients remain asymptomatic in the initial stage of invasive aspergillosis.
Intestinal Transplantation in a Country Without Home Parenteral Nutrition; the Largest Report From the Middle East

Hamed Nikoupour1, Mohammad Bagher Khosravi1, Pooya Vatankhah1, Mohsen Shafiekhani4, Alireza Shamsaeefar2, Peyman Arasteh2, Mohammad Hossein Anbardar4, Mohammad Hossein Eghbal1, Mohammad Ali Sahmeddini1, Fatemeh Khali1, Mohammad Firoozifar2, Samaneh Ghasanfar Tehran1, Saman Nikeghbalian2.

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Background: Many regions of the world, especially middle and low income countries, lack facilities for home parenteral nutrition (HPN) and thus cannot follow existing guidelines for intestinal transplantation (ITx). Inhere we report our experiences with treatment protocols, intraoperative managements, and early postoperative outcomes among patients undergoing either isolated ITx or multivisceral transplantation (MVTx) in our center.

Methods: In the Shiraz Transplant Center, during a one year period from March 2019 up to March 2020, a total of nine ITxs have been performed, including six isolated ITxs and three multivisceral transplantations (MVTx). We reported on donor selection strategies, surgical treatment, anesthesiology care and protocols for total parenteral nutrition, immunosuppression regimen and pathology evaluation.

Results: Mean (SD) age of patients was 37.5 ± 12.5 years. Majority of patients were females (7/9). Median (IQR) waiting time for patients from diagnosis to transplantation 79 (34, 164) days. Our seven day survey of the amount of fluid therapy after transplantation, revealed that the greatest need for fluid therapy was seen on the second postoperative day. After transplantation two patients showed a total of three episodes of severe rejection, one of which was antibody mediated. The one-year survival was 66.6% and the two year survival was 44.5% in our study population. The median (IQR) time to death was 157 (26.5, 382) days. Most common cause of death was sepsis in our series (3/5).

Conclusion: Acceptable outcomes can be obtained with ITx in countries without HPN by application of specific treatment protocols.

Keywords: Intestine; Transplantation; Parenteral nutrition; Anesthesia; Fluid therapy; Autologous gastrointestinal reconstruction.

Table 1. Baseline characteristics and preoperative evaluations among patients with intestinal transplantations.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - yrs</td>
<td>1 2 3 4 5 6 7 8 9</td>
</tr>
<tr>
<td>Sex</td>
<td>F M F M F M F F F</td>
</tr>
<tr>
<td>BMI - kg/m²</td>
<td>17.5 18.7 21.4 13.9 17.3 17.3 16 14.5 19.1</td>
</tr>
<tr>
<td>Underlying disease</td>
<td>A+ O DNM + Optimum additive Liver failure Heart failure CVA Seizure</td>
</tr>
<tr>
<td>Blood group</td>
<td>A+ A+ A+ A+ A+ A+</td>
</tr>
<tr>
<td>Type of surgery</td>
<td>ITx ITx ITx ITx ITx ITx ITx ITx ITx</td>
</tr>
<tr>
<td>Length of TPN - days</td>
<td>360 48 106 22 110 180 35 24 62</td>
</tr>
<tr>
<td>Preoperative evaluation</td>
<td>Normal Normal Normal Normal Normal Normal Normal Normal Normal</td>
</tr>
<tr>
<td>Preoperative evaluation</td>
<td>Normal Normal Normal Normal Normal Normal Normal Normal Normal</td>
</tr>
<tr>
<td>Renal function</td>
<td>Normal IHD Normal Normal Normal Normal Normal Normal Normal</td>
</tr>
<tr>
<td>Pulmonary function</td>
<td>Normal Normal Normal Normal Normal Normal Normal Normal Normal</td>
</tr>
<tr>
<td>Liver function</td>
<td>Normal Normal Normal High enzymes High enzymes High enzymes High enzymes High enzymes</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>Normal Normal Normal Normal Normal Normal Normal Normal Normal</td>
</tr>
<tr>
<td>Viral marker</td>
<td>Neg Neg Neg Neg Neg Neg Neg Neg Neg Neg Neg Neg Neg Neg Neg Neg</td>
</tr>
<tr>
<td>FBS</td>
<td>&gt;120 &gt;120 &gt;120 &gt;120 &gt;120 &gt;120 &gt;120 &gt;120 &gt;120</td>
</tr>
<tr>
<td>Albumin - g/dl</td>
<td>2.5 4.3 3.5 2.1 3.3 2 4 1.5 1.5</td>
</tr>
<tr>
<td>Total bilirubin - mg/dl</td>
<td>1.22 0.22 0.11 0.37 2.25 0.16 0.09 3.24 0.25</td>
</tr>
<tr>
<td>Direct bilirubin - mg/dl</td>
<td>0.38 0.22 0.11 0.37 2.25 0.16 0.09 3.24 0.25</td>
</tr>
<tr>
<td>Creatinine - mg/dl</td>
<td>0.5 0.7 0.6 0.8 0.5 0.9 0.9 0.7 0.5</td>
</tr>
<tr>
<td>Vitamin D level</td>
<td>28.7 106 9.5 5.4 17.9 10.9 17.6 20.9 20.9</td>
</tr>
<tr>
<td>Calcium</td>
<td>Low Low Low Low Low Low Low Low Low</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>Low Low Low Low Low Low Low Low Low</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Low Low Low Low Low Low Low Low Low</td>
</tr>
<tr>
<td>IF:</td>
<td>intestinal failure; TPN: total parenteral nutrition; FBS: fasting blood sugar; HTN: hypertension; DM: diabetes mellitus; IHD: ischemic heart disease; DVT: deep vein thrombosis; CVA: cerebrovascular event; COPD: chronic obstructive pulmonary disease; NET: neuroendocrine tumor; PVT: portal vein thrombosis; ITx: isolated intestinal transplantation; MVTx: multivisceral transplantation</td>
</tr>
</tbody>
</table>

* The normal laboratory range for calcium, phosphorus and magnesium (for males and females) were: 8.6-10.3mg/dl, 2.4-4.5mg/dl and 1.9-2.5 (for males) and 1.8-2.6mg/dl (for females).
<p>| Table 2. Intraoperative assessment and clinical characteristics among patients with intestinal transplantsations. | Table 3. Postoperative assessment and clinical characteristics among patients with intestinal transplantsations. |</p>
<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients</th>
<th>Variables</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid therapy</td>
<td>1 2 3 4 5 6 7 8 9 2</td>
<td><em>Duration of Intubation days</em></td>
<td>2 1 1 1 1 2 1 3 1 9</td>
</tr>
<tr>
<td>Colloid - cc*</td>
<td>3000 2500 2000 2000 1500 500 3000 2500 3000</td>
<td>Duration of admission in ITU days</td>
<td>27 12 15 8 20 17 20 18 20</td>
</tr>
<tr>
<td>Inotropes +</td>
<td>500 - 1000 - 1000 2000 3000 500</td>
<td>Mean received fluid therapy cc/kg/hr</td>
<td>4.39 3.92 2.73 4.90 4.35 4.40 4.81 5.47 4.64 3.7</td>
</tr>
<tr>
<td>Albumin - g</td>
<td>30 - 20 55 5 - 25 30</td>
<td>Fluid therapy on day 1 cc/kg/hr</td>
<td>4.67 3.5 2.1 4.6 3.8 2.1 5.3 4.8 3.7</td>
</tr>
<tr>
<td>UO - cc/kg/hour</td>
<td>3.7 6.9 3.6 2.8 4.5 3.6 2.7 2.7 4.3</td>
<td>Fluid therapy on day 2 cc/kg/hr</td>
<td>5.8 4.2 4.2 6.1 7.2 6.2 7.8 7.4</td>
</tr>
<tr>
<td>Crystallloid index - cc/kg/hour</td>
<td>11.1 11.5 8 8.8 15.7 18.8 13.8 16.9 9.3</td>
<td>Fluid therapy on day 3 cc/kg/hr</td>
<td>3.5 2.6 3.4 4.2 2.9 3.8 5.8 4.1 3.6</td>
</tr>
<tr>
<td>Colloid index - cc/kg/hour</td>
<td>1.8 5 2.0 4 7 3.6 9.2 8.3 2.1</td>
<td>Mean UO</td>
<td>2.4 3.1 2.4 3.5 2.8 3.1 4.6 3.3 3</td>
</tr>
<tr>
<td>Surgery time - hours+</td>
<td>6 4.3 4.3 5 7 5.3 6 6.3 5</td>
<td>Mean albumin - g/dl</td>
<td>2.7 3 2.8 2.2 2.4 2.4 2.4 2.2 2.4</td>
</tr>
<tr>
<td>Blood loss - cc</td>
<td>450 200 500 500 2000 150 800 4700 2000</td>
<td>After reperfusion</td>
<td>PH - mmHg</td>
</tr>
<tr>
<td>Packed cell - bags</td>
<td>1 - - 2 5 - 2 7 5</td>
<td>PCO2 - mmHg</td>
<td>29 33 35 32 36 31 33 38 39</td>
</tr>
<tr>
<td>ROTEM -</td>
<td>Impaired - Normal Normal Normal - Impaired Normal</td>
<td>HCO3 - mmol/L</td>
<td>19.2 23.5 16.3 20.4 19.2 15.8 24 22.6 22.6</td>
</tr>
<tr>
<td>FFP - bags</td>
<td>- 3 - - - - -</td>
<td>BE - mlg/L</td>
<td>-4 -0.2 -10.3 -2.3 -6.4 -8.3 1 -1.7 -3.3</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>- - - - - - - -</td>
<td>Day 1 of ITU admission</td>
<td>PH</td>
</tr>
<tr>
<td>Hemoglobin before surgery - g/dl</td>
<td>10.1 12.4 11.9 9.5 10.6 8.9 13.2 9 7.5</td>
<td>HCO3</td>
<td>7.5 22 18 24.3 14 12.9 16 18.2 1.5</td>
</tr>
<tr>
<td>Hemoglobin start of transplantation - g/dl</td>
<td>11.3 12.5 11.1 11.2 9.7 10 10.4 11.8 10.4</td>
<td>BE</td>
<td>-18 -3 -9 -1.9 -12.3 -13.4 -9.6 -9.6 -8.3</td>
</tr>
<tr>
<td>Plt start of transplantation - *107</td>
<td>150 508 274 363 527 82 220 92 171</td>
<td>Final day of admission</td>
<td>PH</td>
</tr>
<tr>
<td>INR start of transplantation</td>
<td>1 1 1 1.94 1.12 1.6 1.3 1.35 1 1</td>
<td>HCO3</td>
<td>14.6 13.4 18.3 24.5 11.7 23.2 20 28.4 27.8</td>
</tr>
<tr>
<td>Intraoperative medication use</td>
<td></td>
<td>BE</td>
<td>-11.4 -11.7 -9.2 -0.2 -0.2 -0.7 -4.1 4 1 4</td>
</tr>
<tr>
<td>Vancomycin - gr</td>
<td>1 1 1 1 0.5 1 1 1 1 1</td>
<td>Treatment during admission</td>
<td>Dialysis</td>
</tr>
<tr>
<td>Duration of use - days</td>
<td>2 2 2 2 2 2 2 2 2 2</td>
<td>Blood transfusion</td>
<td>- - - - - - - - - -</td>
</tr>
<tr>
<td>Piperacillin - gr</td>
<td>4.5 4.5 4.5 4.5 4.5 4.5 4.5 4.5 4.5 4.5</td>
<td>Inotropes</td>
<td>- - - - - - - - - -</td>
</tr>
<tr>
<td>Duration of use - days</td>
<td>2 2 2 2 2 2 2 2 2 2</td>
<td>Diuretic medication</td>
<td>- - - - - - - - - -</td>
</tr>
<tr>
<td>Methylprednisolone - gr</td>
<td>1 1 1 1 1 1 1 1 1 1</td>
<td>Nutrients on last day of ITU</td>
<td>Calcium</td>
</tr>
<tr>
<td>Duration of use - days</td>
<td>4 4 4 4 4 4 4 4 4 4</td>
<td>Magnesium</td>
<td>Low Low Low Low Low Low Low Low Low</td>
</tr>
<tr>
<td>Diclofenac - mg</td>
<td>500 500 500 500 - 500 500 -</td>
<td>Post-transplantation complication</td>
<td>Mild to moderate rejection no</td>
</tr>
<tr>
<td>Thymoglobulin - gr</td>
<td>50 50 50 50 50 75 50 75 75 75</td>
<td>Severe rejection</td>
<td>0 0 1 1 2 0 0 0 0 0</td>
</tr>
<tr>
<td>Duration of use - days</td>
<td>4 4 4 4 4 4 4 4 4 4</td>
<td>Antibody mediated rejection no</td>
<td>0 0 0 1 0 0 0 0 0 0</td>
</tr>
<tr>
<td>Acid-base treatment</td>
<td></td>
<td>Infection - no.</td>
<td>SSI+UTI+B SI</td>
</tr>
<tr>
<td>Na-HCO3 (7.5%)§</td>
<td>150 150 150 - 350 150 - 200 300</td>
<td>CMV infection</td>
<td>Convulsion - - Pneumonia -</td>
</tr>
<tr>
<td>KCl (15%)</td>
<td>- - - - 10 - 20 5 0</td>
<td>Other complications</td>
<td>Pseudomonas</td>
</tr>
<tr>
<td>U/O: urine output; ROTEM: rotation thromboelastography; FFP: fresh frozen plasma</td>
<td>*This colloid was used gelfusin</td>
<td>GOO</td>
<td>- - - - - - - - - -</td>
</tr>
<tr>
<td>*Surgery time was considered without time of harvest.</td>
<td>*This patient also received 300g/kg octreotide due to underlying NET.</td>
<td>Fistula at site of surgery</td>
<td>Alive</td>
</tr>
<tr>
<td>**It seems that patients with more blood transfusion required more sodium bicarbonate.</td>
<td></td>
<td>Alive</td>
<td>- - - - - - - - - -</td>
</tr>
</tbody>
</table>
Population Model Confirms Predictable Pharmacokinetic (PK) And Pharmacodynamic (PD) Profile for Apraglutide: Data From Two Randomized Phase 1 Studies

Federico Bolognani1, Matthias Machacek2, Annelieke Kruithof3, Matthias Moerland3, Pascal Crenn4, Christian Meyer1, Gerard Greig1, Pim Gal3, Pascal Schulthess2, Marieke de Kam3, Kirsten Bergmann3, Christian Meyer1, Gerard Greig1, Danni Cong2, Niamh Hurley1, Eric Michel1, Nader Youssif1.

Introduction: Patients with intestinal failure associated with short bowel syndrome (SBS-IF) have an increased risk of complications, including renal dysfunction. With currently available glucagon-like peptide-2 (GLP-2) therapy, dosage adjustments are recommended for patients with moderate and severe renal impairment and end-stage renal disease. Apraglutide has unique pharmacokinetic (PK) and pharmacodynamic (PD) properties, with preclinical studies indicating low clearance, slow absorption, and high protein binding resulting in a longer half-life than subcutaneously injected native GLP-2 and other GLP-2 analogs. Apraglutide is degraded into small peptides and amino acids via catabolic pathways, similar to endogenous GLP-2.

Methods: A population PK/PD model was created by combining PK and PD data from two randomized, placebo-controlled, Phase I studies of apraglutide in healthy adult volunteers. In Study 1, 64 volunteers received either a single ascending dose of apraglutide (2.5, 5, 11.4, 28.4, or 56 mg), 3 weekly doses of apraglutide (11.4, 28.4, or 56 mg) or placebo by subcutaneous (SC) injection. In Study 2, 24 volunteers received 6 weekly SC administrations of apraglutide (1, 5 or 10 mg) or placebo. A one-compartmental structural model with zero-order absorption and linear clearance was used to describe apraglutide PK. Plasma citrulline levels were described by a turnover model with a synthesis and degradation rate. The effect of apraglutide on citrulline synthesis was modeled with a stimulatory effect on the citrulline synthesis rate using an Emax relationship. Population PK and PD parameters were estimated using the stochastic approximation of expectation-maximization algorithm (Monolix Suite 2019 R1). Inter-subject variability was modeled using log-normal distributions. Simulations included the impact of covariates.

Results: Actual PK observations were best matched by a population PK/PD model with a dose covariate on absorption duration and body weight covariates on V1/F and Cl/F. The parameter estimates for a 70-kg individual receiving apraglutide 5 mg SC were an apparent volume of distribution of 31.3 L and time to maximal concentration (T) of 1.39 days. Simulated PK and PD observations were best matched by a population PK/PD model with a synthesis and degradation rate. The effect of apraglutide on citrulline synthesis was modeled with a stimulatory effect on the citrulline synthesis rate using an Emax relationship. Population PK and PD parameters were estimated using the stochastic approximation of expectation-maximization algorithm (Monolix Suite 2019 R1). Inter-subject variability was modeled using log-normal distributions. Simulations included the impact of covariates.

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P8.001

Robotic-Assisted Living Donor Nephrectomy: High Technology Incorporated for Patient Benefit

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Background: Kidney transplantation (KT) provides increased survival for patients with end-stage renal disease (ESRD). Living donation (LD) is a cornerstone in the increase of the pool of donors available, especially due to recipients requiring less time on the waitlist and need for ongoing dialysis along with evidence for longer graft survival. One of the barriers for LD is the burden of the procurement surgery, that has traditionally been performed by open or laparoscopic hand-assisted technique. We report here a case series of 22 patients submitted to robotic-assisted left donor nephrectomy.

Methods: Prospectively collected data of patients submitted to robotic-assisted left donor nephrectomies at the Jackson Memorial Hospital, University of Miami, Miami Transplant Institute, in the period of Aug-2021 to Mar-2022, during the first phase of implantation of the Transplant Robotic Program. Data relative to the pre-operative, intra-operative and post-operative periods were collected, including clinic-demographic characteristic of the patients, surgical metrics, and pathology findings. Continuous variables were analyzed with Student t-test, categorical variables were analyzed with chi-square test. A p-value of less than 0.05 was considered to be statistically significant.

Results: 22 patients were included, of those 10 (45.5%) were male. The median age was 40 (30-49.3) years old. Of all cases analyzed, 16 (72.7%) donated the kidney to a related family member. The donor kidney graft anatomy was conventional (single artery, single vein, single ureter) in 19 (86.4%) of the cases. There was 1 (4.5%) case with multiple arteries that was successfully reconstructed in the back-table operation. There were anatomical technical difficulties in 5 (22.7%) cases. A Pfannenstiel incision was used in 10 (45.5%) cases for graft extraction from the abdomen. The median extraction time was 90.5 (IQR 56.5-225.2) seconds. The median intra-operative robotic console time was 102 (IQR 89.8-119.2) min. Robotic stapler devices were used in 21 (95.5%) cases. The median length of stay was 1.23 (IQR 1.0-1.4) days. Graft function was immediate in 20 (90.1%) of the cases, and slow in 2 (9.9%) cases. Macroscopic procurement damage was appreciated in 5 (22.7%) cases. There was 1 (4.5%) postoperative readmission, 4 (18.2%) postoperative complications, and no surgical re-intervention needed. None of the patients had to be converted to laparoscopic or open operation associated to the procedures. There was no statistically significant difference between the groups analyzed.

Conclusion: Robotic-assisted left donor nephrectomy is a safe procedure associated with minor risk of complications, and should be stimulated in the transplant centers where robotic surgery is available.

P8.002

Cholelithiasis: Should We Be More Aggressive in Transplant Patients?

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1Department of Transplantation Surgery, Jackson Memorial Hospital, University of Miami, Miami Transplant Institute, Miami, FL, United States.

Introduction: Symptomatic cholelithiasis is usually a relative indication for cholecystectomy. When acute cholecystitis with potential liver abscess develops in a post-kidney transplant (KT) patient the consequences can be catastrophic, with high risk of graft loss. We report here a case series of 16 patients submitted to robotic-assisted cholecystectomies post-KT due to findings of gallstones or concerning polyps.

Methods: Prospectively collected data of patients submitted to robotic-assisted cholecystectomies at the Jackson Memorial Hospital, University of Miami, Miami Transplant Institute, in the period of Aug-2021 to Mar-2022, during the first phase of implantation of the Transplant Robotic Program. Data relative to the pre-operative, intra-operative and post-operative periods were collected, including clinic-demographic characteristic of the patients, surgical metrics, and pathology findings. Continuous variables were analyzed with Student t-test, categorical variables were analyzed with chi-square test. A p-value of less than 0.05 was considered to be statistically significant.

Results: 16 patients were included, of those 10 (62.5%) were male. The median age was 57 years old (IQR 50-67.8). Of all cases analyzed, 10 (62.5%) were indicated for surgery based on symptomatic cholelithiasis only, 4 (25%) were indicated for surgery based on symptoms of chronic or acute cholecystitis. There were 2 (12.5%) of acute cholecystitis, 2 (12.5%) of chronic cholecystitis, and 2 (12.5%) of gallbladder suspicious polyps. Symptoms were vague and non-specific in 8/10 (80%) of the cases. The median intra-operative robotic console time was 30 min (IQR 23-49). 12 patients presented with intra-operative macroscopic acute/chronic cholecystitis. The median length of stay was 0.9 (IQR 0.9-1.1) days. There were no postoperative readmissions or complications associated to the procedure. The pathology impressively revealed chronic or acute cholecystitis in 15 (93.8%) patients, with no cases of malignancy. There was no statistically significant difference between the groups analyzed.

Conclusion: Immunocompromised patients may not present with classic clinical symptoms. Robotic-assisted cholecystectomy is a relatively simple procedure associated with minor risk of complications, and should be considered for more liberal indication in oligosymptomatic patients.
P8.003

Post-transplant Diabetes de NOVO (NODAT) in a Paraguayan Kidney Transplant Population: Prevalence and Risk Factors

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Introduction and Objectives: NODAT is a well-recognized complication of solid organ transplantation. Its prevalence in Paraguay is unknown. The objective of this study was to determine the prevalence of NODAT in a kidney transplant population of Paraguay and to identify contributing risk factors.

Materials and Methods: Retrospective, descriptive, observational study with an analytical component. From February 2010 to January 2020, 77 first kidney transplants were performed at our institution. The patients included were ≥18 years old, 10 patients were excluded for being DM2. The variables studied were: sex, age, BMI, abdominal circumference, family history of DM2, etiology of CKD, type of donor and immunosuppression used, lipid profile, renal function, and proteinuria at discharge and one year after transplant.

Results: Of the 67 recipients, 49/67 (73.1%) were male, age 45.1 ± 11.6 years; in 36/67 (53.7%) the etiology was unknown, family history of DM2 present in 4/67 (5.9%). The donors were cadaveric in 54/67 (80.5%), tacrolimus (Tac) was the preferred calcineurin in 62/67 (92.5%). Glycemia at 12 months had a significant increase with p= 0.0007. Overweight and type I and II obesity were present in 38.8% and 22.3%, respectively, one year after the transplant and presented a statistically significant difference with the BMI at discharge with a p= 0.0041. The other variables did not present significant differences in the two cuts made. NODAT developed in 10/67 (14.9%) patients; in this population, 89.5% were male, mean age 53.6 years, 85.7% received cadaveric donation, all received CT scan and none had hypomagnesemia. Overweight and type I and II obesity were present in 38.8% and 22.3%, respectively, one year after the transplant and presented a statistically significant difference with the BMI at discharge with a p= 0.0041. The other variables did not present significant differences in the two cuts made. NODAT developed in 10/67 (14.9%) patients; in this population, 89.5% were male, mean age 53.6 years, 85.7% received cadaveric donation, all received CT scan and none had hypomagnesemia. Overweight and type I and II obesity were present in 38.8% and 22.3%, respectively, one year after the transplant and presented a statistically significant difference with the BMI at discharge with a p= 0.0041. The other variables did not present significant differences in the two cuts made.

Conclusion: The prevalence of NODAT was 14.9% in 10 years. Those who developed it were men, with a mean age of 53.1 years, with a transplant from a cadaveric donor and Tac was the most used drug. Most had body mass index of overweight/obesity and hyperlipidemia. There was no correlation with hypomagnesemia. The renal function of the graft was not affected at one year of follow-up in these patients.

Keywords: De novo post-transplant diabetes (NODAT), kidney transplant, tacrolimus.

P8.004

Kidney Graft Surveillance Biopsies, Histological Findings And Safety of the Procedure

Maria Nieves I Aran1, Valeria Albertorto2, Horacio D Curcio1, Sergio Copottelli1, Mari Eugenia Zoppi1, Daniela Wojtowicz1, Rita A Canale1, Florence Williams1, Alejandro Lopez Montero3, Silvia Di Pietrantonio1.

1Nefrología y Trasplante Renal, Hospital El Cruce, Florencio Varela, Argentina; 2Anatomía Patológica, Hospital El Cruce, Florencio Varela, Argentina; 3Diagnóstico por Imágenes, Hospital El Cruce, Florencio Varela, Argentina.

Introduction: Surveillance biopsy is to date, the best available tool to assess the graft’s condition, identifying histological changes before kidney function shows any substantial change. Surveillance biopsy is not a routine practice in many transplant centers; we perform those three months after transplant, in patients with stable kidney function and, one year after transplant, only in special clinical situations. These are performed as an outpatient procedure and with ultrasound guidance.

Methods: 108 surveillance biopsies, performed between October 2016 and January 2022, in patients over 18 years old, who had received kidney transplant (n=99) and liver kidney transplant (n=6) were retrospectively analyzed. Demographic, clinic and laboratory data, pathology reports (categorized according the last Banff classification 2018) and data regarding complications from the procedure, were collected.

Results: 108 kidney graft surveillance biopsies, 6 of them were performed in patients who received combined liver-kidney transplant and 103 in patients who received kidney transplant. 51.85% were men, with a mean age of 43.65 +/- 13.35 (20-75). The mean time between transplant and the biopsy was 5.4 +/- 3.8 months. 74 of them were performed within the stipulated time (3 +/- 2 months), 31 procedures were delayed due to several reasons, such as unavailability, urinary tract infection, anticoagulated patient, COVID pandemic, etc. and 3 second surveillance biopsies performed at 12 +/- 3 months. The mean creatinine at the time of the biopsies was 1.39 +/- 0.54 (0.43-2.98). Histological findings are shown in Figure 1. The number of glomeruli per sample was 22.7 +/- 10.4 (5-67). The mean time between transplant and the biopsy was 5.4 +/- 3.8 months. 74 of them were performed within the stipulated time (3 +/- 2 months), 31 procedures were delayed due to several reasons, such as unavailability, urinary tract infection, anticoagulated patient, COVID pandemic, etc. and 3 second surveillance biopsies performed at 12 +/- 3 months. The mean creatinine at the time of the biopsies was 1.39 +/- 0.54 (0.43-2.98). Histological findings are shown in Figure 1. The number of glomeruli per sample was 22.7 +/- 10.4 (5-67). 5 (4.62%) samples were defined as insufficient (<10 glomeruli). Treatment’s changes occurred, 6 patients with self-limited macroscopic hematuria, 1 of them showed any substantial change. Surveillance biopsy is not a routine practice in many transplant centers; we perform those three months after transplant, in patients with stable kidney function and, one year after transplant, only in special clinical situations. These are performed as an outpatient procedure and with ultrasound guidance. Surveillance biopsy is not a routine practice in many transplant centers; we perform those three months after transplant, in patients with stable kidney function and, one year after transplant, only in special clinical situations. These are performed as an outpatient procedure and with ultrasound guidance.

Conclusion: Kidney graft surveillance biopsy is a valuable tool that is part of the post-transplant follow-up standard, since it is an objective way to systematically demonstrate early histological changes that allow the implementation of prevention and management strategies that impact in the long term outcomes. We believe that the low rate of complications and the number of changes in treatment with diagnosis justify continuing this practice.
Collapsing Glomerulopathy Recurrence in a Kidney Transplant Patient

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Objective: To present a case of recurrent collapsing glomerulopathy after renal transplantation with unclear diagnosis prior to transplantation.

Materials and methods: We reviewed the patient’s medical history as well as the biopsy-reports from native kidneys, whose samples were requested for revision.

Results: 30-year-old male patient with history of nephrotic syndrome with hematuria and hypertension, creatinine of 1.5 mg/dl. The biopsy showed extra-capillary nephropathy with epithelial crescents, he received treatment with corticosteroids and cyclophosphamide, despite of what he evolves with a fall of glomerular filtration rate and dialysis requirement in 2014. In December 2020 the patient receives a kidney transplantation from a deceased donor. He evolved with delayed graft function with dialysis requirement, hypertension and microhematuria. The first biopsy showed borderline cellular rejection; he received treatment with methylprednisolone iv. A second biopsy was performed and it reported nephroangioangiosclerosis and acute tubular necrosis (creatinine 8.07 mg/dl, urea 262 g/dl, and hematuria); subsequently, nitrogen values start to decrease and the patient is discharged. After 45 days, creatinine continued to drop to a minimum of 2 mg/dl and proteinuria began to increase to 15 g/day. After requesting the blocks of the 2014 biopsies for review, we concluded that the course or end stage renal disease was a collapsing glomerulopathy and, in view of the increase in proteinuria (maximum of 15.7 g/dl), we suspected that there was a recurrence of an underlying disease. We performed a third biopsy: glomeruli with hyper trophy and focal podocyte hyperplasia. The patient received treatment with methylprednisolone iv, plasmapheresis and rituximab. Creatinine decreased to 0.9 mg/dl and protein to less than 1 g.

Conclusion: Collapsing glomerulopathy is histologically defined by segmental or global capillary collapse and hyperplasia and hypertrophy of epithelial cells in the urinary space. This exaggerated cellular hyperplasia may resemble a crescent, sometimes leading to misdiagnosis. Recurrences of glomerulopathies in kidney grafts represent a challenge; therefore, knowing the cause of end-stage renal disease prior to transplantation is fundamental to be able to plan ahead these clinical situations.
Urinary Tract Infections in Kidney Transplant. Treatment Duration and Recurrences: A Multicenter Study in Argentina

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Introduction: Urinary tract infections (UTI) are the most frequent infections in kidney transplant (KT). Optimal treatment duration and its relation to recurrence is not clear.

Objective: to analyze treatment duration in relation to recurrence of UTI.

Methods: Retrospective study, in 6 centers in Argentina. All adult KT or combined transplant including kidney that presented UTI and required admission during 2021 were included.

Results: 222 episodes (ep.) in 129 patients (pat.), Sex M 53%, Age: 48(IQR 38-60) KT: 89%, kidney-pancreas 8%, and other 3%. Deceased donor 106 patients, First transplant 91%, 32 pat. (25%) presented previous urolological disorders. 80 pat. (62%) received Thymoglobulin as induction therapy, 32 (24.8%) pat. Basiliximab and 17 (13%) others. Baseline IS was tacrolimus + prednisone + mycophenolate 70%, m-TOR 12 % and other 18%. Microbiology: 126/222 (57%) bacteria were multidrug-resistant organisms (MDRO):E Coli: 95 (42% MDRO); KES: 96 (MDRO 82%), other enterobacteria: 8; Enterococcus 11 P. aeruginosa: 6; Acinetobacter 3, Candida 2. Most pat. with pyelonephritis. Bacteremia was complicated in 32% of cases and 61% of patients had a recurrence.

Conclusions: In this study, recurrence UTI was not related to treatment duration, but our n is too small to assert that correlation, even more among subgroups with different risk factors for recurrence. Due to the importance of antibiotic treatment duration in relation to antimicrobial resistance, it is mandatory to define the optimal treatment duration for UTIs in KT. Our group continues to enroll patients to achieve reliable information.

Recurrences according to treatment duration

<table>
<thead>
<tr>
<th>Previous ATB duration (days)</th>
<th>n</th>
<th>≤ 7 d.</th>
<th>8-10 d</th>
<th>11-14</th>
<th>&gt; 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd ep.</td>
<td>49</td>
<td>31%</td>
<td>18%</td>
<td>47%</td>
<td>4%</td>
</tr>
<tr>
<td>3rd ep.</td>
<td>25</td>
<td>24%</td>
<td>24%</td>
<td>48%</td>
<td>4%</td>
</tr>
<tr>
<td>4th ep.</td>
<td>9</td>
<td>0</td>
<td>33.5%</td>
<td>44.5%</td>
<td>22%</td>
</tr>
<tr>
<td>5th ep.</td>
<td>6</td>
<td>17%</td>
<td>50%</td>
<td>0</td>
<td>33%</td>
</tr>
<tr>
<td>6th ep.</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>100%</td>
<td>0</td>
</tr>
<tr>
<td>1st ep. without recurrence</td>
<td>80</td>
<td>35%</td>
<td>25%</td>
<td>31%</td>
<td>9%</td>
</tr>
</tbody>
</table>
Single Nuclei Profiling of Focal and Segmental Glomerulosclerosis From Human Allografts

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Introduction: FSGS is a complex pattern of injury that can lead to kidney failure and, consequently, end-stage renal disease. It is well known that podocyte injury and loss is a key pathogenic step. Despite concerted research efforts directed at classifying FSGS using a histologic, genetic, or molecular approach, a detailed understanding of the molecular mechanisms of FSGS pathogenesis remain elusive. This study aimed to identify the cellular origin, molecular pathways, and cell-cell interactions contributing to FSGS using a human transplant model.

Methods: Single nuclei RNA-seq was performed on the following human biopsies: i) normal allografts showing non-specific histology (N=4) and ii) FSGS allografts showing glomerular damage (N= 6). Gel-Bead V3 were captured by using the droplet-based 10X Genomic Chromium Platform. Data was analyzed in CellRanger 3.1.0. Downstream analyses were performed including evaluation of cell clusters via uniform manifold approximation and projection, gene and pathway enrichment analyses, intra- and inter-cluster comparative transcriptome analyses.

Results: Using human allografts, a total of 40,078 single nuclei partitioned into 17 unique cell clusters. Stringent quality control metrics were met. We identified both common kidney cell types (e.g. proximal tubular and collecting duct principal cells) and rare cells (e.g. podocytes and immune cells). Comparative analysis between FSGS and normal kidney allografts, revealed both common kidney cell types (e.g. proximal tubular and collecting duct principal cells) and rare cells (e.g. podocytes and immune cells). The podocyte 1 cluster displayed an injured podocyte phenotype enriched in Wnt signaling and actin filament-based pathways. The podocyte 2 cluster displayed a dysfunctional phenotype enriched in ECM deposition, cell morphology, and cell-cell adhesion pathways. Critical, subcluster analysis revealed 10 endothelial cell types, which included glomerular, peritubular capillary, and arteriolar cells, and 6 immune cell clusters, which included macrophages/monocytes, T cells, natural killer cells, and B cells. Immune cells were significantly increased, specifically in T memory cells, and their transcriptional profile was significantly altered in FSGS patients compared to normal.

Conclusions: FSGS is characterized by a complex cellular and transcriptomic landscape, leading to further kidney injury.
The Association of Torque Teno Viral (TTV) Load With Acute Rejection and Viral Infections in the First-Year Post Renal Transplantation

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Introduction: Graft survival after renal transplantation (RT) is mainly determined by rejection and infections complications among others. The individual immune response to the dose of immunosuppressant is highly variable as trough levels are hampered by absorption and metabolism of drugs, and also non-modifiable factors such as age and associated comorbidities that can affect immunity. The non-enveloped DNA non-pathogenic and ubiquitous torque teno virus (TTV) has been postulated as a surrogate marker of immunosuppression in transplant patients. The aim of this study was to evaluate TTV replication as a marker for the appearance of acute rejections or viral infections such as cytomegalovirus (CMV) or BK virus (BKV) after RT.

Methods: This single-center prospective study at CEMIC University Hospital Buenos Aires, Argentina, included 64 patients followed during the first year after transplantation. TTV was detected by real time PCR using primers that amplify a highly conserved region of the 5´non-coding region from all TTV species (Maggi et al., 2003). TTV viral load was quantified on days 0, 3, 7, 14, 21, 30, 90, 180, 360 post-transplantations. Demographics data, clinical and subclinical acute rejection episodes and viral infections (CMV and BKV) detected during the follow-up period were recorded.

Results: The median age was 49.7 years old and 60.3 % were male. Fifty-two patients received a graft from a deceased donor; 98.4 % received thymoglobulin as induction, all patients were on steroids, tacrolimus and mycophenolic acid for maintenance immunosuppression. There were no graft losses and one patient died with a functioning graft within a year after transplantation. TTV was positive in 48/64 (75 %) of patients before transplantation. The median viral load was 2.6 (0.3-3.4) Log10 copies/mL. TTV levels increased rapidly after transplantation. Median viral load +7, +30, +90, +180, and +365 days after transplantation was 3.1, 4.4, 6.5, 5.5 and 5.1 Log10 copies/mL, respectively (p<0.000). On day 90, the prevalence of TTV was 98 %. There was no correlation between Tacrolimus trough levels and TTV throughout the study. During the first-year post-transplantation, 29.7 %, 34.4 %, and 39.7 % had acute rejection, CMV infection, and urine positive BKV, respectively. A total of 15/64 (23.4%) patients presented acute rejection between 3 and 12 months. TTV levels at 6 months were significantly lower in those patients who rejected compared to those who did not; 4.4 vs. 5.9 Log10 copies/mL (p<0.010). The incidence of urological complications and urinary tract infections (UTI) were analyzed and compared between groups. Statistical analysis was performed including the graft and patient survival.

Conclusions: TTV replication increased after RT, reaching the peak on day +90. TTV viral load in this serial quantification a lower viral load at day 180 in patients who presented an acute rejection between 3-to-12-month post transplantation. An association of TTV viral load with viral infections during the first year after RT was observed, although statistically not significant. A higher number of patients are being enrolled for evaluation.

Urological Complications and Urinary Tract Infections Depending on Urinary Outflow in Pediatric Patients After Kidney Transplantation

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Introduction: Kidney transplantation (KTx) is the best option for patients with end stage kidney disease. The group of special consideration are pediatric patients with bladder dysfunction who constitute about 25-35% of all pediatric recipients of kidney transplant.

Objective: The aim of the study was to analyze the occurrence of urological complications (urinoma, ureteral stenosis, renal calculi, vesicoureteral reflux, ureteral necrosis) and urinary tract infections (UTI) depending on urinary solution of urinary outflow (normal bladder vs dysfunctional native bladder vs augmented bladder vs incontinent urinary diversion m.Bricker).

Material and method: Between 2000 and 2020 822 KTx (including 54 reKTx) were performed in our institution. There were 33 Ktx excluded from analysis in patients who were more than 18 years old. Finally 789 KTx were analyzed. Patients were divided into 4 groups: KTx into normal bladder – 538 (group A), augmented bladder - 12group B), dysfunctional native bladder – 150 (group C), incontinent urinary diversion m.Bricker- 89 KTx (group D). In these groups the incidence of urological complications and urinary tract infections were analyzed and compared between groups. Statistical analysis was performed including the graft and patient survival.

Conclusions: Kidney transplantation into the dysfunctional bladder is exposed to the risk of increased frequency of urinary tract infections and urological complications however not diminished survival. Kidney transplantation into incontinent urinary diversion m.Bricker is not associated with increased rate of complications and UTI and should be included in the armamentarium of urinary outflow procedures.
The Impact of a Positive B-Cell Flow Crossmatch in Living Donor Renal Transplant Recipients

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Background: The aim of this study is to determine the incidence of early acute rejection and graft outcomes in living donor renal transplants with an isolated positive B-Cell Flow-Cytometry Crossmatch (B-FCXM).

Methods: We performed a retrospective analysis of graft outcomes in 152 adults who received living donor renal transplants between January 2019 and March 2021 at Mount Sinai Hospital in New York City. Pre-transplant histocompatibility was assessed with flow cytometric crossmatch (FCXM) and Luminex single-antigen beads. Positive B-FCXM was defined as median channel shift of ≥ 40. A mean fluorescence intensity (MFI) ≥ 1400 defined positive donor-specific HLA Class I and/or II antibody (DSA). Most patients received induction immunosuppression consisting of rabbit anti-thymocyte globulin, steroids and intravenous immunoglobulin. Estimated glomerular filtration rate (eGFR) and biopsy-proven rejection at six months’ post-transplant were compared between patients with and without a positive B-FCXM, and positive and negative DSA.

Results: Of 152 patients, 89 (59%) were males and 63 (41%) females; the mean age was 44 years (SD ± 13.8). 45 donor B-FCXMs (30%) were positive and 107 (70%) were negative. 42 (28%) positive donor B-FCXM had no DSA and 3 (2%) had DSA. 91 (65%) negative donor B-FCXM did not have DSA, and 16 (15%) had DSA. Thirty-six (80%) out of 45 patients with positive donor B-FCXM, including the 5 patients with DSA, received intravenous-immunoglobulin (IVIG) as part of induction immunosuppression. None of the patients with both positive donor B-FCXM and DSA had rejection. eGFR and biopsy-proven rejection at six months’ post-transplant were compared between patients with and without a positive B-FCXM, and positive and negative DSA.

Conclusion: In our cohort, there was no statistical difference in early acute rejection and graft function at 6 months between living donor transplant recipients with positive and negative donor B-FCXM even after accounting for DSA status. Per-transplant treatment with IVIG for a positive donor B-FCXM might be a helpful adjunct in this setting.
Kidney Transplantation in Patients With Low MFI Preformed Donor Specific Antibodies

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Introduction: Donor-specific antibodies (DSA) have a central role in the development of acute antibody mediated rejection and chronic allograft nephropathy. Preformed DSA at transplantation, significantly increase risk of antibody-mediated rejection (ABMR). While pre-existing positive DSA with concomitant positive cross-match is a general contra-indication to kidney transplantation, DSA presence with negative crossmatch is still a controversial topic. The presence of DSA with Mean Fluorescence Index (MFI) up to 3,000 and a negative cross-match is not valued as a contraindication to transplantation and is widely accepted. In some transplant centers the chance of transplantation is also offered to DSA positive patients, with MFI up to 5,000. Aim of this study was to analyze graft and patient survival, acute cellular rejection, humoral rejection, renal function and side effects in kidney transplant recipients (KTR) with positive DSA (MFI up to 3,000) and negative cross-match.

Methodology: Nineteen pts (age 53+/-11) with chronic renal failure on chronic hemodialysis treatment (8+/6 years) received a kidney transplant between May 2017 and December 2020. Median PRA was 66%; 100% pts had DSA with average MFI 2122 (min 1039, max 3779). As immunosuppressive therapies all pts received induction with Thymoglobuline plus Rituximab, followed by maintenance immunosuppression with Tacrolimus, MyforticMycoFenolate and Steroids. All patients were on periodic follow up in our Transplant Clinic. Mean follow up was 26.5+/14.4 months. Results were compared to a concomitant KTR group DSA and crossmatch negative.

Results: After 2y follow-up, 17/19 pts are alive (89.5%), one patient died (1/19, 5.2%) because of CMV infection after treatment for ABMR. Three patients returned to dialysis treatment (15.8%) during the first year posttx, because of PNF 1pt, irreversible ABMR rejection 2 pts, 1 other patient had reversible ABMR. Cumulative one year graft survival was 84.2% and the cumulative incidence of ABMR was 15.8%. Average 2 years follow-up creatinine was 1.46+/0.88 mg/dl, median 2 year GFR was 51+/25 ml/min. In the matched control group (19 pts DSA and cross-match negative) 2 years patient survival, graft survival. GFR was not significantly different. Incidence of acute rejection was higher in the DSA positive group (16% vs 0%), but graft loss was not significantly different (16% vs 12%).

Conclusion: Our data suggest that low dose Thymoglobuline plus Rituximab induction allow kidney transplantation in recipient with high PRA (72%) and positive DSA with low MFI (< 3,000), with higher risk of acute rejection, without increasing CMV infection and graft loss.

Prevalence and Risk Factors Associated With Persistent Hyperparathyroidism in Kidney Transplant Recipients

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Introduction: Secondary hyperparathyroidism (HPT) is a frequent complication of end-stage chronic kidney disease (CKD). HPT normally remits around the first year after a successful kidney transplant (KT), correcting most of the metabolic abnormalities; however, it persists in 15 to 50%, called Persistent Hyperparathyroidism (pHPT), increasing the risk of loss of bone mass and fractures. Several factors may be associated with development of pHPT, but so far, they are not well defined. In addition, there is no consensus to define the levels of iPTH to establish pHPT. The KDIGO guidelines recommend starting treatment when the iPTH is >100 pg/ml.

Objectives: To evaluate the prevalence of pHPT in the first year after KT and to correlate it with calcaemia (Ca), phosphatemia (P), alkaline phosphatase (AP) and renal function. Evaluate risk factors for the development of pHPT.

Materials and methods: An observational, longitudinal and retrospective study was carried out in patients who received KT from the Nephrology Service of Córdoba’s Hospital between 2010 and 2019. The data were obtained from the medical records of Nephrology Service. Most received induction with basiliximab and an immunosuppressive regimen with calcineurin inhibitors, mycophenolate, and steroids. The variables analyzed were: age of the organ recipient, sex, type of donor, etiology of CKD, the modality and time on dialysis. The levels of iPTH, Ca, P and AP were recorded at the time of KT, at 6 and 12 months. Renal function was evaluated at 1, 6 and 12 months. Descriptive statistics were used for the analysis. The comparison between the groups was made using the Chi-square test and the t-test, considering p-value <0.05 significant.

Results: A total of 48 patients were included, the prevalent etiology of CKD was unknown (31%), followed by nephroangiosclerosis (19%). The mean age of the patients was 42.0 ± 11.8 years, 54% were male, 25 patients had PTH before KT (PTH >300 pg/ml, 52%). A total of 10 patients, 20%, most of them women, presented pHPT one year after KT. The longer stay on dialysis (47.9 vs 85.6 months; p<0.01) and the older age of the recipient (40.3 vs 48.7 years; p<0.003) were associated with the development of pHPT. Other risk factors associated with this development were higher levels of AP and iPTH at 6 months post-KT (see Figure 1 A and 2 B). They also presented a propensity for hypercalcaemia (10.5 vs 9.6 mg/dl) and hypophosphatemia (2.5 vs 3.5 mg/dl). One year after of KT, 70% of all patients had GFR between 30-60 ml/min and 30% >60 ml/min, however renal function was similar in both groups.

Conclusion: The most important risk factors for the development of pHPT post-KT were patient’s age, time on dialysis, AP and iPTH levels at 6 months post-KT. Resolution of HPT occurred in 80% after one-year post KT. Future strategies should be focus on shortening time in waiting list and the timely treatment of tertiary HPT prior to transplantation.
Gram Negative Blood Stream Infection in Renal Transplant Recipients: Risk Factors and Outcome From a Transplant Center in Pakistan

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Background: Gram-negative bacteremia (GNB) is a common cause of bloodstream infection in renal transplant recipients (RTR). The risk factors are cytomegalovirus infection (CMV), pre-transplant dialysis, acute rejection, urological abnormalities, and ureteral stent. The mortality rate is 2.5 to 11%. Considering the huge impact on morbidity and mortality, our aim is to analyze the characteristics and outcomes of GNB in RTRs.

Methods: A case-control study at Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan. The files of all renal transplant recipients who had documented GNB from January 2015 to December 2017 were reviewed till December 2020. The controls were matched with age, sex, and date of transplant. The first episode of GNB was taken. Clinical features, received anti-thymocyte globulin (ATG) or solumederol and cytomegalovirus infection (CMV) 90 days pre or post bacteremia, recurrent urinary tract infections (UTI), source of bacteremia and microbiology, all-cause mortality at day 28 and graft function at the last follow up were noted.

Results: Out of 1009 RTR, 33 (3.3%) episodes of GNB occurred. The mean age was 30±11.85 years, 61% males. Around 48% developed bacteremia within 6 months post-transplant. The most common source was UTI (75.8%). Fever in 48% and only 39% had leukocytosis. Around 9% were admitted in the intensive care unit. E-coli was the most common organism (70%) (Table 1).

Stone disease at the time of transplant was significantly associated with bacteremia (p=0.029). There was no difference in receiving ATG or solumederol and CMV before bacteremia. A significant number of patients received solumederol for rejection (p=0.035) and had CMV (p=0.044) within 90 days after bacteremia. Recurrent UTI is significantly associated with bacteremia (p<0.001). The graft function at the last follow-up (2 years) was significantly deranged in patients with bacteremia (p=0.0001).

Conclusion: Gram-negative bacteremia was found in 3% of RTR and half of them developed within 6 months post-transplant. UTI was the most common source and recurrent UTI was significantly associated with bacteremia. The stone disease was the most significant risk factor. Patients develop rejection and CMV infection within 3 months post bacteremia. There was a significant graft dysfunction among patients with bacteremia at a mean follow-up of 2 years. We need to focus on the management of recurrent UTIs to prevent bacteremia and graft dysfunction in renal transplant recipients.
Post Renal Transplant Malignancy: Single Center Experience

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Introduction: Kidney transplantation in patients with end-stage kidney disease improves quality of life and is associated with an increase in survival rates. Malignancies are one of the three major causes of renal recipient’s death with a functioning graft after cardiovascular diseases and infections. The incidence of post-transplant malignancies (PTM) varies between 2.0 and 30%, depending on the characteristics of the population.

Aim of study: The aim of this study is to analyze the incidence of PTM in solid organs and organs with hematological origin, excluding non-melanoma skin tumors, in kidney transplant recipients, as well as to evaluate factors associated with global survival in a single center.

Materials and methods: Retrospective observational cohort study. Data of 2,146 medical records that underwent kidney transplantation from deceased or living donors between 2000 and 2015 were analyzed.

Results: The cumulative incidence of PTM de novo was 5.5% with a mean follow-up of 9 years. During this period, 118 cases of PTM were reported, 103 in solid organ and 15 with hematological origin. The most frequent malignancy was kidney cancer, followed by malignant lung, prostate cancer and non-Hodgkin lymphoma. Patients who developed PTM had a lower overall survival compared to those without malignancy (12.2 vs 18.2 years, p <0.001), and for recipients with PTM of hematological origin, mortality was higher in relation to those with solid organ neoplasms (p = 0.03). PTM is an independent risk factor for death in the post-transplant period (HR = 4.75, 95% CI: 3.52 –6.42; p <0.001), as well as the age of the recipient and donor above 60 years.

Conclusion: The incidence of renal PTM was 5.5%, with renal neoplasia being the most frequent. PTM was an independent prognostic factor for the patient’s death, being that of hematological origin associated with higher mortality.

Table 1: Characteristics of patients with GNR bacteremia, n=33

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Case (33)</th>
<th>CONTROL (44)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years) Mean ± SD</td>
<td>40±11.5</td>
<td>29±11.2</td>
<td>0.79</td>
</tr>
<tr>
<td>Male</td>
<td>29 (87.9%)</td>
<td>45 (68.2%)</td>
<td>0.444</td>
</tr>
<tr>
<td>HLA Matching</td>
<td>Good</td>
<td>25 (75.8%)</td>
<td>41 (61.7%)</td>
</tr>
<tr>
<td>Bad</td>
<td>2 (6.1%)</td>
<td>1 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>Identical</td>
<td>6 (18.2%)</td>
<td>14 (21.2%)</td>
<td></td>
</tr>
<tr>
<td>Primary Bacteremia</td>
<td>Gram-positive</td>
<td>13 (39.4%)</td>
<td>16 (24.2%)</td>
</tr>
<tr>
<td>Staphylococcus</td>
<td>5 (15.2%)</td>
<td>2 (3.0%)</td>
<td>0.038</td>
</tr>
<tr>
<td>Unknown</td>
<td>21 (63.6%)</td>
<td>40 (59.1%)</td>
<td>0.029</td>
</tr>
<tr>
<td>Other</td>
<td>1 (3.0%)</td>
<td>1 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>CMV within 90 days after bacteremia</td>
<td>3 (9.1%)</td>
<td>5 (7.6%)</td>
<td>0.516</td>
</tr>
<tr>
<td>CMV within 90 days after bacteremia</td>
<td>3 (9.1%)</td>
<td>6 (9.1%)</td>
<td>0.655</td>
</tr>
<tr>
<td>Immunosuppressive regimen at the time of transplant</td>
<td>Cyclosporine based</td>
<td>52 (78.8%)</td>
<td>52 (78.8%)</td>
</tr>
<tr>
<td>Tocilizumab based</td>
<td>6 (18.2%)</td>
<td>14 (20.2%)</td>
<td>0.723</td>
</tr>
<tr>
<td>Mycophenolate Mofetil based</td>
<td>5 (15.2%)</td>
<td>4 (22.2%)</td>
<td>0.674</td>
</tr>
<tr>
<td>Azathioprine based</td>
<td>27 (81.8%)</td>
<td>58 (87.9%)</td>
<td>0.415</td>
</tr>
<tr>
<td>Antimicrobial Prophylaxis received at the time of transplant</td>
<td>Amoxicillin-clavulanic acid</td>
<td>30 (84.8%)</td>
<td>29 (84.8%)</td>
</tr>
<tr>
<td>Aztreonam-Imipenem</td>
<td>5 (15.2%)</td>
<td>7 (10.9%)</td>
<td></td>
</tr>
<tr>
<td>Recurrent UTI before bacteremia</td>
<td>5 (15.2%)</td>
<td>20 (45.5%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>CMV within 60 days before bacteremia</td>
<td>18 (54.5%)</td>
<td>18 (40.9%)</td>
<td>0.199</td>
</tr>
<tr>
<td>Graft function at follow up median (IQR)</td>
<td>1 (0.01-1.5)</td>
<td>1 (0.9-1.5)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Table 2: Composition of GNR Bacteremia and Control
Human Leukocyte Antigen Tissue Typing in a Guatemalan Transplant Center

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Introduction: The Kidney Transplant Program at the Hospital General San Juan de Dios (HGSJDD) began in 1992, to date more than 700 transplants have been performed, of these only 15% were from cadaveric sources. The Histocompatibility and Immunogenetics Laboratory, was funded in 2012 as part of the Nephrology and Transplant Department, back in that year tissue typing was performed by Complement Dependent Cytotoxicity (CDC), spanning the last decade the laboratory implemented other tissue typing techniques and anti-HLA antibody analysis, which represented an important advance for the transplant program and the country of Guatemala, since it is the only public laboratory that performs molecular biology and Luminex techniques. Herein we present the preliminary findings of HLA-A, B, DRβ1 and DQβ1 tissue typing using an SSOP-PCR based technique in 127 patients at the HGSJDD Kidney Transplant Program.

Methods: 127 patients from the HGSJDD Kidney Transplant Program were recruited from January 2018 to December 2020, unrelated to each other, without a known diagnosis of diseases mediated by the major histocompatibility complex, and 100% self-identified as mestizos, all agreed to participate; the research was approved by the ethics and research committee of the HGSJDD and was conducted in accordance with the Helsinki Declaration principles. HLA genotyping was performed using a PCR-SSOP Luminex® method. HLA-A~B~DRβ1~DQβ1 allelic and haplotypic frequencies of 127 subjects were calculated using the Arlequin® v. 3.5 software.

Results: We found 194 haplotypes among the studied population, 16 of which presented a frequency greater than 1%, those 16 represent 39.7% of the total haplotype diversity. All found haplotypes had been previously described in Latin American populations, 13 of the haplotypes found had been reported in Native American populations. This is the first time that an HLA genes allele and haplotypic frequencies study has been carried out in Guatemalan mixed population. The most frequently found haplotype was HLA-A*02~B*35~DRβ1*04~DQβ1*03:02 (9.06%). The allelic and haplotypic frequencies were stored on: www.allelefrequencies.net database and can be accessed under the identification number (AFND-ID: 3743).

Conclusions: The results of this study constitute a valuable tool for transplantologists in Guatemala, since knowing the immunogenetics of the Guatemalan population allows them to assess better options for patients in cadaveric source programs, in order to find a compatible donor, and to evaluate in advance the immunosuppression strategies that can benefit them, according to the immunological risk that they present. It also allows to establish the initial steps for the medium-term implementation of paired donor and/ or domino program, in order to exchange organs between hospitals, that will to start organ procurement programs. There are no previous works, describing HLA genes tissue typing in mestizo Guatemalan population.

Improving Access to Kidney Transplantation: Waitlisting And Kidney Transplantation in Southeastern Brazil

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Introduction: Brazil holds the largest public transplant system globally. The State of Minas Gerais has the second-highest burden of end-stage renal disease (ESRD) in the Southeastern region of Brazil. Still, it holds seventh place in the number of kidney transplants. It is crucial to understand barriers to increasing the number of dialysis patients who get waitlisted for a transplant.

Setting & Participants: 23,927 incidents patients (2015-2019) who received chronic hemodialysis therapy for at least 90 days in Minas Gerais were identified within the DATASUS System and National transplant System (SNT) at 84 dialysis facilities and followed through September 2020.

Outcomes: Waitlisting and transplanting

ANALYTICAL APPROACH: Multivariable time-dependent Cox models for the incident population.

Results: Among 23,927 adult patients on incident dialysis, 3,442 (14%) were listed and 1,211 (4.4%) transplanted in six years. Factors significantly associated with a lower waitlisting and transplantation (p < 0.0001) included non-profit status dialysis facilities, female gender, >60 years old and treatment in the south part of the state.

Conclusion: Geographic differences across the state can identify opportunities to increase funding for healthcare resources in proportion to patient and disease burdens. Transplant centers must assist underserved populations in ensuring equity in access to services. Policies that improve patient access to care are essential to alleviate geographic disparities.
Incidence and Correlates of Testicular Pain After Kidney Donation

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Introduction: Testicular pain after kidney donation is often understudied with previous literature reporting on less than 100 total cases. Herein, we describe the incidence of testicular pain after kidney donation in 2551 kidney donors and explore factors associated with its development.

Methods: We evaluated the presence of testicular pain in a retrospective cohort study of kidney donors who donated between 1963 to 2007 at three US transplant centers as part of The Renal and Lung Living Donor Evaluation Study. Univariate, bivariate and multivariate generalized linear model (GLM) were used to determine factors associated with having testicular pain.

Results: Of the 2551 male donors, 54 (2.12%) developed testicular pain 19 days (IQR 7, 40) after donation: 34 had testicular pain only, 6 had epididymitis, and 14 had both. Donors developing pain were 4 years older and pain occurred more often in those undergoing laparoscopic nephrectomy: 3.6% vs. 1.1% for open nephrectomy. Post-donation testicular pain was more likely to be experienced by non-Hispanic White donors; RR 5.56 (95% CI 1.35, 22.84), p=0.02 and those undergoing laparoscopic nephrectomy; RR 3.11 (95% CI 1.71, 5.65), p<0.001. Neither laterality of the kidney removed nor the number of renal arteries in the donated kidney were associated with having testicular pain. Factors associated with its development differed by gender. Women were more likely to experience testicular pain regardless of their ethnic background. While men were more likely to have testicular pain if they underwent laparoscopic nephrectomy. The incidence of testicular pain was 3.6% vs. 1.1% for open nephrectomy. Post-donation testicular pain was more likely to be experienced by non-Hispanic White donors; RR 5.56 (95% CI 1.35, 22.84), p=0.02 and those undergoing laparoscopic nephrectomy; RR 3.11 (95% CI 1.71, 5.65), p<0.001. Neither laterality of the kidney removed nor the number of renal arteries in the donated kidney were associated with having testicular pain.

Conclusions: The incidence of testicular pain was 3.6% vs. 1.1% for open nephrectomy. Post-donation testicular pain was more likely to be experienced by non-Hispanic White donors; RR 5.56 (95% CI 1.35, 22.84), p=0.02 and those undergoing laparoscopic nephrectomy; RR 3.11 (95% CI 1.71, 5.65), p<0.001. Neither laterality of the kidney removed nor the number of renal arteries in the donated kidney were associated with having testicular pain. Factors associated with its development differed by gender. Women were more likely to experience testicular pain regardless of their ethnic background. While men were more likely to have testicular pain if they underwent laparoscopic nephrectomy. The incidence of testicular pain was 3.6% vs. 1.1% for open nephrectomy. Post-donation testicular pain was more likely to be experienced by non-Hispanic White donors; RR 5.56 (95% CI 1.35, 22.84), p=0.02 and those undergoing laparoscopic nephrectomy; RR 3.11 (95% CI 1.71, 5.65), p<0.001. Neither laterality of the kidney removed nor the number of renal arteries in the donated kidney were associated with having testicular pain.

Study the Effect of Sodium-Glucose Cotransporter-2 Inhibition Versus Dipeptidyl Peptidase-4 Inhibition in Diabetic Kidney Transplant Recipients

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Introduction: Diabetes is the most common cause of chronic kidney disease (CKD) globally. The renal and cardiovascular benefits of the new antidiabetic agents are not assessed comprehensively.

Aim of the study: We aimed to evaluate the short-term renal and cardiovascular effects of Sodium-Glucose Cotransporter-2 inhibition (SGLT2) Vs. Dipeptidyl peptidase-4 inhibition (DPP4i) among diabetic kidney transplant recipients.

Patients and methods: In this observational trial, 222 diabetic kidney transplant recipients (NODAT or type 2 diabetes) were enrolled and were categorized into two groups. Group 1 (n=99) received SGLT2 while group 2(n=123) received DPP4i as an add on antidiabetic medications. All patients in the two groups were followed up for 12 months.

Results: Most patients in the two groups (1&2) were men (59.6 vs. 61.7%, p=0.73) in their middle age (58.5±11.9 vs. 54.4±12.9, p=0.016) years respectively. The two groups were matched regarding their demographics especially the type of donor, type of immunosuppression (induction or maintenance), number of cardiovascular events before enrollment in the study, and the number of patients who were maintained on ACEI or ARB(p>0.05). The minority of patients were smokers (12.9 vs.8.7%), and chronic glomerulonephritis was the original disease in 36.4 vs. 35.4% in the two groups, respectively. Most of the enrolled patients (72.8 vs. 78.6%) underwent hemodialysis pre-transplant. During the follow-up period, patients in both groups were comparable regarding mean blood pressure, body weight, HbA1C, 24-hour urine protein, and graft function (represented by the mean serum creatinine) at different time intervals and compared to baseline values(p>0.05). However, the mean HbA1C was significantly higher in group 1 during the whole follow-up period of the study (p=0.05) but it did not drop significantly compared to baseline values(p>0.05). We did not report any macroangioplastic events (cerebral stroke, acute myocardial infarction, or peripheral arterial disease) in the two groups during the study.

Conclusion: Both GLT2 and DPP-4 I are comparable regarding renal and cardiovascular protection among diabetic kidney transplant recipients.

Keywords: DM, renal protection, kidney transplant
Structured Diabetes Education: Significance Among Kidney Transplant Recipients With Post-transplant Diabetes

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Introduction: Diabetes knowledge among kidney transplant recipients with post-transplant diabetes (NODAT) is not evaluated comprehensively.

Aim of the study: We aimed to evaluate the impact of structured diabetes education on the development of diabetic micro- and macro-angiopathies in kidney transplant recipients with new-onset diabetes after transplant.

Patients and methods: In this prospective randomized controlled trial, we categorized 210 kidney transplant recipients with NODAT into two groups according to the type of diabetes education (in a ratio of 2:1). Group 1 (n=140) received structured diabetes education while group 2 (n=70) received conventional education.

We collected patients’ data in patient identification and metabolic control parameters.

Results: Most patients in the two groups (1&2) were Kuwaiti (60.7 vs. 58.6%), men (57.9 vs. 68.6%), with high school education levels (43.6 vs. 48.6%). The minority of patients were smokers (12.9 vs. 8.7%), and chronic glomerulonephritis was the original disease in 36.4 vs. 35.4% in the two groups, respectively. Most of the enrolled patients (72.8 vs. 78.6%) underwent hemodialysis pre-transplant. At the start of the study, the percentage of patients with diabetic neuropathy was comparable in both groups (32.4 vs. 27.6% in the two groups respectively) and after 24 months, follow-up electromyography/nerve conduction did not show a significant difference between the studied groups (p>0.05). Similarly, the number of patients with fundus imaging showing retinopathy was comparable in both groups at the study’s start and end (p>0.05). Also, macroangiopathic events (cerebral stroke, acute myocardial infection, or peripheral arterial disease) were higher in group 1 but did not rank to significance (p>0.05). On the other hand, although the percentage of patients with nephropathy was comparable in both groups at the start of the study, this percentage decreased significantly in group 1 after 24 months of the study compared to group 2 and the basal value in the same group (p=0.016).

Conclusion: Structured diabetes education is associated with reducing diabetic nephropathy but without significant impact on other micro- or macroangiopathy. We recommended being delivered to all diabetic kidney transplant recipients.

Acute Kidney Injury Among COVID-19 Positive Patients Is Associated With Higher Mortality: Single Center Experience

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Introduction: Despite the lungs being the major targets of COVID-19, other organs such as the kidneys are also affected. Renal complications of COVID-19 are not yet well studied.

Aim: We aimed to study the prevalence of acute kidney injury (AKI) among positive COVID-19 cases that were managed in the intensive care unit (ICU) in a single isolation hospital during the pandemic, and to explore its impact on patient outcome.

Methods: This retrospective study included 616 patients with COVID-19 who were managed in the ICU in a single isolation hospital in Kuwait during the pandemic, from February to December 2020. AKI was defined according to the serum creatinine criteria in the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. Of the 616 patients, 40.2% developed AKI (group 1, n=248) and were compared with the patients without AKI (group 2, n=368).

Results: Most of the cases in the 2 groups were males (73% vs. 70.7%), aged (60.8± 14 vs. 51.7± 16 years) respectively. The 2 groups were comparable regarding chronic kidney disease (2% vs. 0.8%), and chronic pulmonary disease. Other factors were significantly predominating among group 1 as diabetes mellitus (63.7 vs. 40.5%), hypertension (74.2% vs. 40.5%), ischemic heart disease (26.2% vs. 12.5%); also cases who received supportive vasopressors and convalescent plasma transfusion, as well as steroids, were significantly higher among the AKI group (p<0.05). Moreover, sepsis, volume depletion, shock, arrhythmias, and ARDS predominated among the AKI group (P<0.05). The number of cases that were managed by therapeutic anticoagulation was significantly higher in AKI patients (89.9 % vs. 51.9%); also cases who received supportive vasopressors and convalescent plasma transfusion, as well as steroids, were significantly higher in the same group (p<0.05). Other therapeutic modalities such as antivirals, tocilizumab, and hydroxychloroquine were comparable in both groups. We found that acute respiratory failure requiring mechanical ventilation was significant among the AKI group (66.8% vs. 29.4%), and the overall mortality rate was significantly higher in the same group (62.5%, vs. 32.8%).

Conclusion: The prevalence of AKI in patients with COVID-19 was 40.2%, and it was associated with poor prognosis among ICU covid-19 positive cases.
P6.024

Evaluation of Function of Angiopoietins and ANIOPOIETIN Likes in Post-transplantation Diabetes Mellitus (PTDM) in Kuwaiti Kidney Transplanted Patients

Mohamed J. Jahromi2, Torki Al-Otaibi1, Osama Gheith1,3, Nashwa Othman2,3, Tarek Mahmoud1, Parasad Nair1, Medhat A. Halim1, Mohamed Abu Farha2, Jihad Abu Baker2.

Background: Post Transplantation Diabetes Melliteus (PTDM) is a chronic metabolic disease developed in some of our kidney transplant patients. PTDM is a chronic, inflammatory disease with a direct impact on patients’ immune system. Angiopoietin and Angiopoietin-like are intrinsic mediators induced by immune cells.

Objectives: To determine the relationship between circulating Angiopoietin-1 and 2 (ANG-1, 2) and Angiopoietin-like (ANGPTL 3-8) in kidney transplant patients who develop diabetes (PTDM) vs. patients who do not develop diabetes (CONTROL) after kidney transplantation.

Methods: In this cross-sectional study, all patients were enrolled from Dasman Diabetes Institute Diabetes Education Department and outpatient clinics of the Hamad Al Essa Organ Transplant Centre of Kuwait between May 2015 and December 2016. The present study included 155 PTDM and 154 controls, age- and sex-matched. We collected 3ml of venous blood from each subject. Enzyme-linked immunosorbent assay (ELISA) determined plasma ANG 1,2 and ANGPTL 3-8. We determined the correlation between plasma ANG 1 and 2 and ANGPTL3-8 levels in our PTDM and Control group.

Results: In our cohorts, most of the patients (56%) were Kuwaiti. Moreover, the two groups were comparable regarding their original kidney disease, dialysis type, donor type, and the type of both induction and maintenance immunosuppression (P > 0.05). Also, pre-transplant co-morbidities were comparable in both groups, including hypertension, history of exposure to tuberculosis bacilli, ischemic heart disease, bone disease, anemia, and hyperlipidemia (P > 0.05). We found significantly higher plasma ANG-1, ANGPTNL 6, 7, 8 levels in the PTDM group compared to the control group (P < 0.001), However, we found no statistical association between our study groups concerning plasma ANG 2, ANGPTNL 3, 4 (p>0.05).

Conclusion: Plasma ANG 1, ANGPTNLE, 7, 8 levels may correlate with disease severity, chronicity in transplant patients who develop diabetes post Kidney transplantation, and serve as a potential biomarker of the disease severity.

Key Word: Angiopoietin; Angiopoietin Like, Kidney Transplantation, PTDM, ELISA

P6.025

Impact of Full Correction of Post-transplant Anemia on the Cardiovascular System in Renal Transplant Recipients Receiving Erythropoietin Stimulating Agents: Prospective Randomized Controlled Trial

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Objectives: Several studies have shown that PTA might be associated with increased mortality and decreased graft survival and de-novo congestive heart failure.

Aim of the study: So we aimed from this prospective randomized controlled study to assess the impact of full correction of post-transplant anemia on the cardiovascular system of renal transplant recipients receiving erythropoietin stimulating agents.

Patient and methods: We recruited 247 kidney recipients with stable graft function in this RCT with 2 groups according to their target hemoglobin (11-12 g/dl, group 1, n=183) and (13:15 g/dl, group 2, n=64). After correction of deficiencies, the target hemoglobin was achieved using ESA. All patients were followed up clinically and by serum creatinine and eGFR monthly for 12 months.

Results: Diabetic nephropathy was the main cause of ESKD in group 1 (p=0.005). The studied groups were comparable regarding pre-transplant co-morbidities. Most patients received thymoglobulin as induction then cyclosporine-based maintenance immunosuppression. We did not find any significant difference between the two groups concerning post-transplant diabetes, BK viremia or malignancies, and even cardiovascular events (TIA, stroke, ACS), uncontrolled hypertension, heart failure, or arrhythmias (p>0.05). Group 1 showed higher mean blood pressure (p=0.003), low LV internal dimensions, higher LVH, LV mass, IVSD, and LV mass index after one year of the study (p<0.05). Group 2 did not show any significant change in the same parameters (p >0.05). Moreover, IVSD, mean ejection fraction, and FS were comparable in both groups (p>0.05). Graft outcome was comparable between both groups (p=0.005).

Conclusion: Full correction of PTA is associated with stabilized cardiac dimensions indices without any significant cardiovascular co-morbidities.
P8.026

Contrast-Induced Nephropathy in Kidney Transplant Recipients: A Single-Center Experience

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Introduction: Although published papers studying contrast-induced nephropathy (CIN) in native kidneys are abundant in the medical literature, data related to CIN in renal allografts are relatively rare. Moreover, kidney transplants are at higher risk for developing CIN due to unique factors to renal allografts as immunosuppressive agents, lack of sympathetic denervation, glomerular hyperfiltration, and burden of cardiovascular disease.

Aim of the study: To determine the prevalence of contrast-induced nephropathy among renal transplant recipients who received low-osmolality iodine-based contrast material before radiological assessment.

Patients and methods: Out of 3180 renal transplants, which are followed up in Hamed Al-Essa organ transplant center, 79 patients received low osmolality iodine-based contrast before radiological assessment for different indications during the period between 2010 and 2020. According to our protocol, all patients received pre-contrast precautions (to hold metformin, IV hydration, sodium bicarbonate, and N acetylcysteine). CIN was defined when serum creatinine rose by 25% from baseline within one week of contrast exposure. Risk factors of CIN were assessed.

Results: Seventy-nine patients were enrolled for statistical analyses and divided into groups 1(CIN, N=7) and 2(control, N=72) without any early rise of serum creatinine. The mean age was 52.1±12.3years, 44 of them were males, most of them reached ESKD due to diabetic nephropathy. The pre-transplant co-morbidities, virology status, and HLA typing were comparable in the two groups. Forty-seven cases received contrast for coronary angiography, while 32 received it for CT studies. Post-transplant ischemic heart disease (P 0.03) was significantly higher among group 1(N=46). The renal function deteriorated among CIN patients, especially after one week and four weeks, but the renal function between the two groups was comparable at the end of the study.

Conclusion: CIN is not uncommon in renal transplant recipients receiving CM especially ischemic heart disease recipients. Risk stratification, optimize hemodynamics and avoid potential nephro-toxins in transplant recipients planned to receive contrast-enhanced trials. Prospective controlled trials of CIN in transplant settings are justified.

P8.027

Idiopathic Polymyositis in Renal Transplant Recipient: Case Report and Review of Literature

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Introduction and aim: Myositis is a rare complication following renal transplant and is most commonly the result of a drug-mediated myotoxicity, but the idiopathic cause is still the most common. After kidney transplant, the differential diagnosis of polymyositis includes autoimmune disease, drug-induced viral infections, and rhabdomyolysis associated with electrolyte imbalance. We aimed to report a case of idiopathic polymyositis in a renal transplant recipient and review the literature for similar cases.

Case report: A 31-year-old male patient developed polymyositis three years following live-related kidney transplantation. Electromyography confirmed myopathic changes. The clinical features and course, MRI findings, EMG features, positive anti-MI-2 antibody, and the response to high-dose steroid therapy are matched with immune-mediated acute polymyositis, especially after excluding viral infections and drug-induced myopathy.

Conclusion: Acute polymyositis may occur after a kidney transplant. Possible mechanisms include viral antigen transmission or a localized graft vs. host disease. Muscle biopsy is not mandatory before prompt initiation of high-dose steroid therapy, which leads to clinical and biochemical recovery. Keywords: Polymyositis, kidney transplant, outcome
Impact of Autophagy on the Development of Senescence in Protocol Biopsies in Kidney Transplant Patients

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Introduction: In kidney transplant, the expression of cyclin-dependent kinase inhibitors p16INK4a, a cellular senescence marker, is a strong predictor of poor allograft outcome. Autophagy is a tightly regulated cellular self-degradation recycling process characterized by sequestration of damage organelles in double-membrane vesicles called autophagosomes, as a cellular survival mechanism under stress. VMP1 vacuole membrane protein1 is a transmembrane protein involved in the initial steps of the autophagy process. Patients with chronic allograft dysfunction have downregulation of autophagy. Both senescence and autophagy are activated in response to kidney injury during transplantation. A relationship between both seems to exist, although it is still poorly understood, and human studies are scarce. A better understanding of this phenomena could allow the development of therapies to increase graft longevity. We aim to assess the relationship between senescence and autophagy through tissue expression of p16INK4a and VMP1 in renal transplants patients.

Materials and Methods: Protocol transplant (Tx) kidney biopsies at zero hour, 1 and 12 post Tx months in patients who consent were included. Immunohistochemistry staining for p16 INK4a was performed on paraffin biopsy sections with peroxidase anti-peroxidase Ventana BENCHMARK-XT. Immunofluorescence with antibodies to Polyclonal rabbit antiserum to VMP1 were used. We evaluated the extent of nuclear p16INK4a staining and VMP1 positive expression as a punctate cytoplasmic structure in the renal cortex. Semiquantitative scoring of p16INK4a and VMP1 staining intensity (1-3; 3 representing maximum intensity) was analyzed.

Results: 12 protocol biopsies from 4 cadaveric kidney tx patients were analyzed. All patients had triple immunosuppressive regimen and none had rejection in the biopsies. VMP1 was negative in glomeruli (podocyte, endothelial and mesangial cell) in all biopsies. In VMP1 positive samples, it was found as granular intracytoplasmic vacuole in proximal and distal tubule cells and in arterial smooth muscle cells. Nuclear p16INK4a staining was positive in proximal tubules and glomerular endothelial cells. Semiquantitative scoring of p16INK4a and VMP1 staining intensity (1-3; 3 representing maximum intensity) was analyzed.

Conclusion: In renal biopsies from 4 kidney Tx patients, those who expressed the cell-protective autophagy marker VMP1 did not express the senescence marker p16 INK4a.

Table 1: Semiquantitative scoring of p16INK4a and VMP1 staining intensity (0-3; 3 representing maximum intensity)

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<tr>
<th>Patient</th>
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Mini-Flank Donor Nephrectomy Incision: A Single Centre Experience From Nigeria

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Background: Kidney transplantation in sub-saharan Africa is in the rudimentary stages. Majority of patients with chronic kidney disease have no access to renal replacement therapy and hence die from the disease. Donor nephrectomy (DN) is an important aspect of kidney transplantation. It entails safe retrieval of a healthy renal allograft from a donor for this purpose. Over the last 2 decades, open DN has given way to minimal invasive techniques like laparoscopic and robotic DN. However, DN via a mini-incision has gained popularity in many parts of the world as a suitable alternative to LDN especially where there are lack of facilities or expertise for LDN or robotic DN. Mini-incision donor nephrectomy (MIDN) is a modification of the ODN with incisions of<12cm in length and has been found to offer an acceptable scar, duration of hospital stay, pain assessment and generally less morbidity than with the traditional ODN. This study aims to describe our experience with mini-flank incision DN among Nigerian patients.

Patients and Methods: A prospective review of all donor nephrectomy patients performed in a single Nigerian kidney transplantation centre over a 30-months duration was made. Information obtained from these patients were classified as pre-, intra- and post-operative. Data include socio-demographic characteristics, pre-operative preparation, details of intra-operative findings eg post-operative pain, days on admission, analgesic requirements, duration of ileus, commencement of oral intake and cosmetic outlook of the scar. These were entered into a proforma and analyzed using SPSS version 21.

Results: A total of 304 patients underwent ODN during the study period, of which 230 (75.6%) had MIDN. Mean duration of the surgery was 130±28 minutes MIDN was mostly performed on patients with BMI of <30kg/msq and these patients had better post-operative pain control. Oral intake and ambulation was commenced on 1st day post-op and the cosmetic outcome was acceptable in over 90% of kidney donors.

Conclusion: Mini-incision for Donor Nephrectomy through the flank approach is a suitable alternative to laparoscopic donor nephrectomy in the developing world were facilities and skills for laparoscopic or robotic nephrectomies are unavailable. It offers shorter operating time and 1st warm ischemic time with comparable morbidity rate.

Key words: Renal transplantation, Donor Nephrectomy, Mini incision, Nigeria

Post-kidney Transplant Prospective Comparison of Measured Urinary Creatinine Clearance With Estimated -eGFR Based on Serum Creatinine or Kinetic- KeGFR for Rapid Changes in Serum Creatinine

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Introduction: Post kidney transplant (KTx) with functioning renal allograft, serum creatinine continues to decrease at a variable rate until it stabilizes. Currently, the Cockcroft- Gault (C-G) and Modification of Diet in Renal Disease MDRD-4 formulae, and are based on a single serum creatinine value to estimate GFR for chronic kidney disease. For rapid changes in serum creatinine, the kinetic estimated GFR (KeGFR) formula was developed for recovering acute kidney injury. However, post-KTxs with functioning allograft eGFR and KeGFR formulae/ calculators’ values are not compared with measured urinary creatinine clearance by any glomerular isotope excretion methods. Hence, the medications requiring dose adjustment based on renal function might not be adjusted appropriately. The aim of the present study is to compare actual urinary creatinine clearance every 12 hours with C-G, MDRD-4, and (KeGFR) after functional KTx.

Patient and method: 34 consenting subjects (mean age 55.2 +/- 13.8 years; 14 male) were enrolled of which 24 had immediate primary allograft function. These were prospectively studied under IRB-approved protocol. Urine was collected every 12 hours through a Foley catheter post-KTx until serum creatinine was stabilized. Creatinine clearance was calculated [U (urinary creatinine) x V (urinary volume)]/ S (serum creatinine); (UV/S). Over 200 creatinine clearance values were compared with C-G, MDRD-4, and Chen’s KeGFR calculator at 12, 24- and 48-hours intervals.

Results: At each time point, the measured urinary creatinine clearance was consistently higher compared with eGFR by C-G, MDRD-4 formula, and KeGFR by Chen calculator until serum creatinine was stabilized around 2mg/dL (Figure-1). The mean creatinine clearance was 68.1 ± 22.1 mL/min. Twenty-two (91%) subjects had a urinary creatinine clearance >50 mL/min and 18 (81%) had a creatinine clearance >60 mL/min. Both eGFR and KeGFR were not compared with actual urinary creatinine clearance.

Conclusion: Our prospective observations suggest that eGFR by C-G, MDRD-4, and KeGFR at 12, 24, and 48 hours, underestimate the GFR compared to urinary creatinine clearance for post-KTx function of allograft recipients. We suggest adjusting post-KTx medications based on a 50% decrease in pre-transplant serum creatinine, where measured urinary creatinine clearance is >50mL/min in 92% of cases and >60mL/min in 81% of cases. Renally dosed medication could be adjusted with a 50% decrease in serum creatinine in post-KTx. Future studies are required with exogenous glomerular filtration markers for more accurate formulae with functioning allografts in the immediate post-KTx period.

Reference:
**P8.031**

**Outcome of Simultaneous Pancreas Kidney Transplantation: A Single Center Experience**

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Introduction: Simultaneous transplantation of pancreas-kidney (SPK) transplantation is one of the treatment options for type 1 diabetes mellitus (T1DM) patients with chronic kidney disease stage 5. The SPK outcomes reported in the literature are excellent with a 5 year patient, kidney and pancreas graft survival of 88%, 77% and 69% respectively. Here, we present our data regarding the outcome of the SPKT done at our institution.

Method: We studied patients who underwent SPKT in our institution. 11 T1DM patients who were CKD-5 underwent SPKT from 2014 to 2022. Their graft function and complications were analysed.

Results: A total of 12 patients were studied. 50% were males and 50% were females. Mean age at diagnosis was 14 ± 4 years. Mean age at transplantation was 32 ± 6 years. Mean hemodialysis (HD) vintage was 22 ± 14 months. Mean age of donor was 31 ± 10 years. Induction was with Basiliximab in 1 patient, Alemtuzumab in 5 patients and ATG in 6 patients. Maintenance immunosuppression was tacrolimus and mycophenolate in 8 patients; and, tacrolimus, mycophenolate and everolimus in 2 patients. Mean duration of hospital stay was 30 ± 18 days. Mean graft kidney function at 1 month was 1.38 ± 0.48 mg/dl. Mean graft kidney function at 6 months was 1.30 ± 0.47 mg/dl. At 1 year, one patient had severe renal graft dysfunction requiring HD. Among the other 10 patients who completed one year, mean kidney graft function at 1 year was 1.25 ± 0.23 mg/dl. Three (25%) patients had renal allograft loss with need for initiation of HD after 30, 21 and 6 months. Two patients with renal allograft loss required insulin after 19 and 25 months. Three (25%) patients had delayed graft function. Five (41.7%) patients had renal allograft rejection at 1 month. Among the five, three had another episode of rejection at 17, 11 and 4 months. Three (25%) patients had suspected pancreatic graft rejection at POD 13, 13 and 14, which resolved with intravenous steroids. Eight (66.6%) patients had infections in the first year following transplant which included urosepsis, LRTI, tuberculosis, varicella, CMV, cellulitis, periodontal abscess, dental caries and esophageal candidiasis. Seven (58.3%) had surgical complications including pseudo aneurysm of graft pancreas, urinoma, perinephric hematoma, abdominal bleed and DIC, jejuno-jejunal anastomotic site bleed, kinked renal vein requiring re-exploration, graft pancreas fat necrosis with impending GB rupture and peritonitis, and splenic vein thrombosis requiring re-exploration. Other complications noted were incisional hernia, subacute intestinal obstruction, bilateral femoral head avascular necrosis and acute myeloid leukemia.

Conclusion: The graft survival and outcomes in our institution is comparable to that of international standards. Surgical complications were noted to be higher compared to renal transplantation. SPK remains to be treatment of choice in T1DM patients with ESRD.

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**P8.032**

**Post-transplant Malignancy Amongst Kidney Transplant Recipients: A Single Centre 20-Year Experience and Literature Review**

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Materials and Methods: We analysed our data retrospectively which included 794 patients who underwent renal transplantation at our centre between January 2002 to February 2022. Patients’ native kidney disease, donor details, duration on hemodialysis, immunosuppression details and duration till diagnosis of malignancies were collected. All details regarding the nature of the malignancy with detailed histopathology, staging, and treatment were also collected. We also done subgroup analysis of multiorgan, liver and hand transplant recipients.

Results: Of the total 794 cases of renal transplant recipients, 15 recipient (1.7%) were diagnosed with malignancy. Seven out of the 15 patients were males (46%). The mean age at diagnosis was 41±10 years and mean duration of occurrence of malignancy following post transplant was 38 months. Eight patients(46%) developed solid organ tumour and 7 (54%) developed post-transplant lymphoproliferative disease. Of the eight cases of solid organ tumors, 4 had squamous cell carcinoma of the tongue followed by one case each of adenocarcinoma of the pancreas, adenocarcinoma of colon and squamous cell carcinoma of the lung and vulva. Seven out of 15 patients succumbed to their malignancy, a mortality rate of 46%. Of the seven cases of PTLD, 6 had expired(86%), making PTLD the most fatal post-transplant malignancy in our setting. Of the 794 post-kidney transplant cases reviewed in this single centre retrospective study, the incidence of malignancy was 1.8 per 100 population. At our centre, there was a prevalence of PTLD as the major type of post-transplant malignancy, as compared to studies from other centers. PTLD being of poor prognosis, is responsible for a higher post-transplant mortality rate of 54% in our population. The most aggressive histopathological variant of PTLD (Monomorphous variant) was common in our cohort. This may represent either an ethnic predisposition to this disease or some environmental or immunological risk factors contributing to its occurrence.

Conclusion: This study points out the need for meticulous surveillance of all post-transplant cases for malignancy considering the associated high rate of mortality.
P8.033
Teriparatide in Kidney Transplant Patients With Bisphosphonate-Resistant Osteoporosis
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1Kidney Transplant, Nephrology-ITAC, Caba, Argentina.

Introduction: Bisphosphonates increase Bone mineral density (BMD) by suppressing bone turnover inhibiting osteoclastic function with risk of inducing adynamic bone disease. Teriparatide is a fragment of the natural human parathyroid hormone (PTH) consisting of the first 34 amino acids counting from the N-terminus end of the natural PTH. Is anabolic drugs stimulate bone formation by increasing osteoblast activity and regulates both bone formation and resorption reducing the risk of vertebral and nonvertebral fractures. Aim: Teriparatide (Parathormone 1-34) treatment in renal transplant patients with bisphosphonate-resistant osteoporosis.Methods: observational describe study of cases series of 10 kidney transplant patients with bone fragility without response to prolonged treatment with bisphosphonates (greater than 3 years). They were treated with daily subcutaneous injections of 20 microg teriparatide (PTH 1-34) by 18 months. All the patients had 6 months of bisphosphonate wash out. Measurements: we investigated bone turnover markers and effect of teriparatide over BMD of the femoral neck and lumbar spine as well also fractures, graft rejection, cardiovascular events, death and drug related adverse event.

Results: 10 patients 9 women, mean age 64.4±14.15 years, BMI 24.3 ±2.6, etiology 3GMN, 3 PKD, 3 unknown, 1 NDBT, HD 9, preemptive 1, transplant Time 10.12±5.21 years, 1 preemptive, 8 DBD and 1 LRD, Induction: 8 thymoglobulin, 2 basiliximab, Maintenance 5 belatacept/mycophenolate/MTP, 2 rapamune/mycophenolate/MTP, 3 tacrolimus/mycophenolate/MTP, 6 patients with fractures prior to treatment. Mean of treatment with 1-34 PTH increased levels of bone alkaline phosphatase (13.26 U/L ± 5.75 vs 17.90 ± 7.28, p = 0.045), with NS changes in the rest of the analytes (Table 1) and increase of lumbar bone density of 11.27% (0.8816 gr/cm2(TS-2.5) vs 0.7230 gr/cm2(TS-2.19)).

Measurements: we investigated bone turnover markers and effect of teriparatide over BMD of the femoral neck and lumbar spine as well also fractures, graft rejection, cardiovascular events, death and drug related adverse event.

Discussion: Our results are consistent with the literature, showing that teriparatide increased bone density of the lumbar spine and femoral neck compared to baseline. This increase was accompanied by a significant decrease in Bone turnover markers, suggesting a beneficial effect of teriparatide on bone turnover.

Conclusion: In this group of patients, and adequate response to teriparatide treatment was observed however our limitation was small number of patients and bone biopsy prior teriparatide treatment.

<table>
<thead>
<tr>
<th></th>
<th>VR (n=10)</th>
<th>18 M (n=10)</th>
<th>p (.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum bALP, U/L</td>
<td>11.95</td>
<td>13.26±5.75</td>
<td>17.90±7.28</td>
</tr>
<tr>
<td>**Serum OC, mg/m</td>
<td>13.43</td>
<td>14.81±20.44</td>
<td>15.08±15.52</td>
</tr>
<tr>
<td>***Serum B-CTX,</td>
<td>300-570</td>
<td>395.22±207.35</td>
<td>402.66±115.59</td>
</tr>
<tr>
<td>mg/ml</td>
<td>uCa, mg/dl</td>
<td>100-300</td>
<td>110.66±40.93</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>0.6-1.10</td>
<td>0.9±0.28</td>
<td>1.0±0.35</td>
</tr>
<tr>
<td>PROT/24hs</td>
<td>0.0-0.14</td>
<td>0.11±0.13</td>
<td>0.08±0.10</td>
</tr>
<tr>
<td>IP/TH, pg/ml</td>
<td>15.45</td>
<td>54.44±42.64</td>
<td>72.35±53.62</td>
</tr>
<tr>
<td>Z/CRP, ng/ml</td>
<td>&gt;40</td>
<td>42.22±24.51</td>
<td>34.71±12.80</td>
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<tr>
<td>ICA, mmol/L</td>
<td>2.8-5</td>
<td>4.13±0.70</td>
<td>4.27±0.52</td>
</tr>
<tr>
<td>P, mmol/L</td>
<td>2.3-4.7</td>
<td>3.72±0.84</td>
<td>3.32±0.35</td>
</tr>
<tr>
<td>Mg, neq/L</td>
<td>1.3-2.10</td>
<td>1.48±0.27</td>
<td>1.55±0.22</td>
</tr>
<tr>
<td>CHOLESTEROL, mg/dl</td>
<td>&lt;200</td>
<td>205.22±35.96</td>
<td>214.22±40.47</td>
</tr>
<tr>
<td>BUN, mg/dl</td>
<td>3.5-7.2</td>
<td>4.51±0.41</td>
<td>5.03±1.10</td>
</tr>
<tr>
<td>Lumbar spineBMD,</td>
<td>0.68±0.22</td>
<td>0.99±0.171</td>
<td>0.07</td>
</tr>
<tr>
<td>femoral neck BMD</td>
<td>0.675±0.08</td>
<td>0.723±0.08</td>
<td>0.09</td>
</tr>
</tbody>
</table>

*Bone-specific alkaline phosphatase
**Obinutuzumab
***Beta Cross Laps

P8.034
Single Port Robotic Versus Open Kidney Transplantation: A Comparison of Outcomes
Alvin C. Wess1,2, Mohamed Eltemamy1,2, Aaron Kavianini2, Yi-Chia Lin1,2, Mahmoud Abou Zeinab1, Alp Tunca Bekscak1, Ethan Ferguson2, Jihad Kaouki2
1Tranplant Center, Cleveland Clinic, Cleveland, OH, United States; 2Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH, United States.

Introduction and Objective: We introduced the single-port robot-assisted kidney transplantation (KTP) using the da Vinci SP platform in 2019. Herein, we aimed to compare the perioperative and follow-up outcomes of the initial series of patients who underwent this procedure with the standard open KTP.

Methods: We compared a prospective cohort of 12 patients who underwent SP robotic KTP from Oct 2019 to Oct 2021 with a retrospective cohort of 12 matched patients who had open KTP at our institute. Patients were matched for donor type, the kidney donor profile index (KDI) in deceased donors, recipient age, and history of diabetes. Perioperative data were retrieved from our institutional review board (IRB) approved database. Normality of data was tested with the Kolmogorov-Smirnov test when indicated. The comparison of normal data was performed using a T-test. Comparison of percentiles was performed using the "N*" Chi-squared test.

Results: Baseline characteristics and perioperative data of these patients are presented in table 1. No patients in SP arm were converted to open surgery. Mean (SD) revascularization time in SP and open arms were 72.75 (11.93) and 36.25 (9.39) minutes respectively (P < 0.0001). There were no intra or postoperative complications greater than Clavien grade 2 in either group. The morphine milligram equivalents (MME) score during admission was 44.91 (40.15) in SP and 149.16 (119.70) in open groups (P = 0.0091). 6-, and 12-month graft and patient survival were 100% in both arms. There was no significant difference in mean creatinine level at 1, 6, and 12 months between SP vs. open group. There were no vascular or surgical complications during follow-up in either arm.

Conclusion: Single port robotic kidney transplantation offers a minimally invasive approach with similar safety and allograft function compared to open kidney transplantation with the added benefit of less postoperative narcotics requirement. Larger series are required in this setting.
P8.035

Early Recovery After Surgery Program in Kidney Transplantation Patients: Comparison of Clinical Outcomes With Conventional Care Program

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Purpose: Early recovery after surgery protocols (ERAS) has been adopted in many surgical procedures. Transplant ERAS (T-ERAS) is a peritransplant multimodal approach aimed at shortening recovery and improving outcomes. T-ERAS has been introduced into our institution since 2018 and becomes the standard of care for kidney transplantation. We aimed to report the difference between T-ERAS and conventional pathway at our institution.

Methods: We retrospectively reviewed 817 patients who had kidney transplantation only in our department from 2015 to 2020. Patients were divided into Group 1 from 2015 to 2017 (n=369) and Group 2 from 2018 to 2020 (n=448).

Results: Patients in Group 2 were older (56 vs 53 years, p<0.01) and had less living donation (32.3% vs 44.6%, P<0.01). Patients in Group 2 had a lower rate of delayed graft function (DGF) (8% vs 16.8%, P<0.01) decreased length of stay (3 vs 5 days, P<0.01) with a higher creatinine level at discharge (3 vs 2 mg/dl, P<0.01) but similar creatinine levels (p=0.1) and better graft survival at 6 months (99.3% vs 96.5%, P<0.01).

Conclusion: The T-ERAS protocol was associated with a lower rate of DGF, decreased length of hospital stay and better graft survival at 6 months. The higher creatinine at discharge can be explained by the larger percentage of living donation in Group 1 as well as the earlier discharge.

<table>
<thead>
<tr>
<th>Recipient Characteristics</th>
<th>Group 1 (n=369)</th>
<th>Group 2 (n=448)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53 [40-62]</td>
<td>56 [46-65]</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>142 (38.5)</td>
<td>171 (38.2)</td>
<td>0.92</td>
</tr>
<tr>
<td>Body mass index, kg/m2</td>
<td>28.4 [24.3-32.7]</td>
<td>28.3 [24.2-32.2]</td>
<td>0.91</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td>0.55</td>
</tr>
<tr>
<td>White, %</td>
<td>254 (68.7)</td>
<td>317 (70.6)</td>
<td>0.67</td>
</tr>
<tr>
<td>African American, %</td>
<td>89 (24.1)</td>
<td>94 (20.9)</td>
<td>0.34</td>
</tr>
<tr>
<td>Hispanic</td>
<td>9 (2.4)</td>
<td>8 (1.8)</td>
<td>0.34</td>
</tr>
<tr>
<td>Asian</td>
<td>5 (1.4)</td>
<td>12 (2.7)</td>
<td>0.21</td>
</tr>
<tr>
<td>Middle east</td>
<td>10 (2.7)</td>
<td>16 (3.6)</td>
<td>0.18</td>
</tr>
<tr>
<td>Other</td>
<td>3 (0.8)</td>
<td>2 (0.5)</td>
<td>0.55</td>
</tr>
</tbody>
</table>

| Cause of renal failure    |                |                | 0.07 |
| Diabtes                   | 77 (20.6)      | 121 (27.0)     | 0.31 |
| Glomerulopathy            | 74 (20.0)      | 82 (18.3)      | 0.34 |
| Hypertension              | 57 (15.4)      | 79 (17.6)      | 0.31 |
| Re-transplant             | 49 (13.2)      | 30 (6.7)       | 0.01 |
| PKD                       | 20 (5.4)       | 40 (8.9)       | 0.01 |
| Other                     | 93 (25.2)      | 97 (21.5)      | 0.31 |

| Pre transplant dialysis   | 287 (80.3)     | 346 (77.1)     | 0.31 |
| Waiting time, months      | 15.6 [6.4-36.9] | 13.8 [4.8-38.9] | 0.31 |

| Donor Characteristics     |                |                | 0.01 |
| Live donor                | 165 (44.6)     | 145 (32.3)     | < 0.01 |
| Deceased donor            | 205 (55.4)     | 304 (67.7)     | 0.01 |

| Postoperative outcome     |                |                | 0.01 |
| First week dialysis       | 62 (16.8)      | 36 (8.0)       | < 0.01 |
| Length of stay, days      | 5 [4-7]        | 3 [2-4]        | < 0.01 |
| Serum creatinine at discharge, mg/dl | 2.0 [1.3-4.4] | 3.0 [1.7-5.1] | < 0.01 |
| Graft status at 6 months, alive | 357 (98.5) | 440 (99.3) | < 0.01 |
| Serum creatinine at 6 months, mg/dl | 1.4 [1.1-1.7] | 1.3 [1.1-1.6] | 0.1 |

NOTE: Continuous variables: median [IQR]; Categorical variable: number (%)

P8.036

Late Humoral Rejection: Will Temporality Be Enough To Determine the Therapeutic Attitude?

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Introduction: Antibody-mediated rejection (AMR) is the main cause of graft loss, but current guidelines only recommend optimization of immunosuppression in late AMR (>30 days post-transplantation). This study assesses the effectiveness of treatment in late AMR, as well as the responses between clinical rejections and those detected by protocol biopsy.

Materials and Methods: Retrospective cohort of kidney transplant recipients with AMR under follow-up at the INCMNSZ and the “CMN20 de Noviembre”, between January 2011 and March 2021. Chi square and Student’s T or Mann-Whitney U were used according to their distribution. Spearman’s correlation was used. A p <0.05 was considered significative.

Results: 180 patients were analyzed, 57.2% women, average age 35.9 years, 65.6% living donor, 33% received Thymoglobulin as induction and 66.7% received prednisone, mycophenolate and tacrolimus. 95% were late AMR. 65% detected with protocol biopsy. Class II DSA predominated. The evolution of the glomerular filtration rate (GFR) is shown in figure 1, without difference between early and late AMR. The overall response rate to treatment (GFR maintained or returned within 25% of baseline) immediately, at 1, 6, and 12 months was 73%, 69%, 59%, and 59%, respectively. No difference in GFR for those with and without a response. There was no correlation between the inflammation score (G+ptc) with the GFR in any period. There was an inverse correlation between the chronicity score (ci+ct+cg+cv) and the GFR at diagnosis, at the end of treatment, at 1 and 12 months (-0.261, -0.261, -0.237 and -0.146, respectively).

Conclusions: There were not differences in the response to treatment between early or late AMR and should not determine the therapeutic attitude. Protocol biopsies detected more than half of AMR, demonstrating its relevance.
**P8.037**  
**Changes in Body Composition After Renal Transplant in Children**  
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¹Unidad de Investigación en Nefrología y Metabolismo Mineral Óseo, Hospital Infantil de México Federico Gómez, Mexico, Mexico; ²Unidad de Epidemiología Clínica, Hospital Infantil de México Federico Gómez, Mexico, Mexico.  

**Introduction:** Due to the relationship between adipose tissue and cardiovascular outcomes, it is important to monitor the changes in body composition after renal transplant. The aim of the study was to describe the changes in body composition in children during the first-year post-renal transplant.  

**Methods:** We included a cohort of patients aged 5-18 years transplanted between 2014-2017, all signed informed consent/assent. A dual-energy X-ray absorptiometry (DXA) and anthropometric measurement was performed in the first three months after renal transplant and 12 months afterwards. Bone mineral content (BMC), fat mass (FM), non-bone lean mass (LM) and the index lean mass/Fat mass was calculated to evaluate the proportion of lean mass related to fat.  

**Results:** 50 patients were included, 51% males, 69% adolescents. At baseline low height was found in 78%; by body mass index 69% were normal, 14% had overweight, 4% obesity and 12% were emaciated. By body composition median FM was 26% for female children, 27% for males; in adolescents it was 34% for females and 22% for males. At 12 months the frequency of subjects with normal weight increased to 80%, diminishing the frequency of overweight to 12% and obesity to 2%, only 6% continue emaciated. The changes in the body fat percentage in males was -0.01% whereas in females increased 0.03%, p>0.05.  

**Conclusions:** It is important to evaluate body composition changes in pediatric renal transplant receptors, we found that they continue with low height. No significant changes were found at 12 months in BF/LM in Mexican transplanted children. Adolescent women tend to acquire more fat.  

**Financed by Fondos Federales 2014/009.**

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**P8.038**  
**Prevalence of Genetic Mutations Associated With Kidney Disorders in Renal Transplant Recipients – Single Centre Experience**  
Ankur Mittal¹, Abhijit Konnur¹, Sishir Gang¹, Mohan Rajapurkar¹, Umapati Hegde¹, Hardik Patel¹, Shaleesh Soni², Sachidanand Panday².  
¹Nephrology, Muljibhai Patel Urological hospital, Nadiad, India; ²Pathology, Muljibhai Patel Urological hospital, Nadiad, India.  

**Introduction:** End-stage renal disease (ESRD) of undetermined etiology is highly prevalent and constitutes a significant clinical challenge, particularly in the context of kidney transplantation. Underlying renal conditions leading to ESRD are extremely heterogeneous and the prevalence of hereditary nephropathies among adults with ESRD is less known. To date, less than 10% of adult ESRD is thought to be genetic. Genetic analysis often reveals the cause of kidney failure in patients with unknown kidney disease. For patients awaiting renal transplantation, genetic testing prior to kidney transplant may help to understand the outcome in these patients. We studied the prevalence of genetic mutations related to kidney disease in renal transplant (RTx) recipients.  

**Methods:** It was a Single Centre, Observational, Cohort Study. Between October 2019 & July 2021, 123 RTx recipients were analyzed using Multiplex Ligation-dependent Probe Amplification (MLPA) and clinical exome sequencing for mutations related to kidney disease.  

**Results:** Mean age was 36±12 years, 96 (78%) were Males. 88 (71.5%) were undetermined and 35 (28.4%) had established cause of CKD. 8 patients had structural or hereditary kidney disease and 27 were non-hereditary including DKD, Glomerulopathy, Obstructive uropathy and CTID diagnosed by kidney biopsy and clinical and radiological presentations. 17/88 (19.3%) patients with undetermined CKD on renal biopsy showed Glomerulosclerosis (6), CGN (8) & TMA (2), one had advanced renal damage. 32/88 (36.36%) patients had genetic mutations related to kidney disease. 20 were structural congenital or hereditary kidney disease & 10 had a mutation for Glomerulopathies. Mutations related to complement regulatory genes were found in 84/123 (68.2%). 6 patients had congenital or hereditary kidney disease, 12 were DKD, 5 were Glomerulopathy, 2 had Obstructive Kidney disease and 1 had CTID. Homozygosity and heterozygosity were seen in 14 (16.8%) and 10 (12%) patients respectively. 67/88 (90.7%) also showed CFHR1/CFHR3 gene complex duplication, reported as a variant of uncertain significance. 1 patient had a mutation for the PLG gene, previously been implicated in the pathogenesis of ahus.  

**Conclusion:** This study demonstrates 82.9% (102/123) prevalence of the genetic mutation in RTx recipients. Genetic analysis provides the etiology in 35 patients with undetermined kidney disease. The significance of complementary regulatory gene related mutation remained uncertain.
Allele, Genotype and Haplotype Frequencies of the HLA System in the Province of Neuquén, Argentina

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1Laboratorio Central, Subsecretaria de Salud, Neuquen, Argentina.

Knowledge of the bioanthropological and genetic characteristics of the population in Neuquén is limited. Determination of the allele and haplotype frequencies of the HLA system provides data on genetic variability, susceptibility or resistance to diverse disease, immunological phenomena and contributes to the selection of donors and recipients in organ transplantation.

583 samples from patients attending the histocompatibility laboratory between January 2015 and March 2022 have been analyzed retrospectively. HLA typing of locus A, B and DR has been performed on all patients by using medium resolution ssop methodology (sequence specific oligonucleotide probes).

It was observed that, in locus A, the predominant allele was A2, with a frequency of 15.5 (42.8%). It was followed by A68, with a frequency of 12.22 (33.2%) and A24, with a frequency of 6.83 (20.8%). In locus B, the majority alleles were B35 and B39, with a frequency of 2.68 (33.3%). They were followed by B7, with a frequency of 2.89 (13.8%) and B40, with a frequency of 2.68 (12.8%). In locus DR, the most frequent allele was DR4, with a frequency of 20.85 (46.5%). The second most frequent allele was DR11, with 9.23 (20.6%), and finally, DR8, with 9.0 (20%).

The most frequent genotype in locus A was A2-A68 (9.77%). In locus B, it was B35-B39 (5.83%) and, in locus DR, it was DR4-DR4 (7.55%).

The most frequent haplotypes were A2-B39 (15%) and A68-B39 (13.4%). Regarding loci A-B-DR, the most observed haplotype was A68-B39-DR4 (7.5%).

Due to the existing demographic growth in the province, according to the last census, Neuquén received population from the whole country (Argentina) and from South American countries. Even though the most frequent alleles were similar to alleles from other studies conducted, substantial discrepancies were also identified. Thus, considering the great number of native peoples present in Neuquén, using these methodologies for the study of closed populations would be convenient in the future.

Baradello Stefano.
Vascular Surgeon in Transplantation Team, Is There a Room For Such Specialist?

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Renal transplant is the best solution for treatment patients with chronic renal failure. Five year survival of patients after kidney transplant is 85% comparing to hemodialysis 35%. Peripheral arterial disease is present in 45-50% of recipients. Significant PAD could be contra-indication for renal transplant and arteriosclerosis disease can lead loss of transplanted organ during operation, acute limb ischemia, renal artery stenosis, renal HTN. Optimisation of conditions for transplant is the key for success. Many transplant centers qualify recipient to renal transplant with examining patients with Doppler ultrasound and if doubt performing CTA. Doppler ultrasound has less sensitivity and much less specificity comparing to CTA (91 vs 95% and 86 vs 96%). Vascular complications occurs 1.29-4.4% kidney transplants and are 3-15% of the cases of graft dysfunction. Most common vascular complications are transplanted renal artery stenos, transplant arterial and venous thrombosis, arteriovenous fistula (AVF) or intra-renal pseudo-aneurysm or extra-renal pseudo-aneurysm. Transplanted renal stenosis is the most common and could be situated in suture site due to technical problems, lesion of the proximal renal artery caused by perfusion or organ harvesting, recipient arterial stenosis due to clamp or arteriosclerotic disease. Arterial thrombosis usually resulting graft loss is usually occur due to technical complications during transplantation or harvesting, technical problems during performing anastomosis, torsion or kinking artery. Renal vein thrombosis could be also associated by technical problems during transplantation, perigraft fluid or vein compression. Other vascular complications such as acute limb ischemia caused by thrombus, resection, septic bleeding from inflamed vessels usually required vascular surgeon assist. We have reviewed 124 kidney transplants done between 2017 to 2021. We observed that taking part of vascular surgeon or cardiac surgeon (during his training for specialty in transplantology) could caused significant (15-19 %) less vesicular complications comparing to control group, more significant in group of recipients with higher risk of vascular complications, arteriosclerotic disease. Post transplant complications such as transplant artery stenosis were successfully treated by endovascular procedures (angioplasty) or open repair as well as arterial or venous trombectomies. Artery dissection, septic bleeding following inflammation and more complicated procedures like reconstruction of vessels with recipients veins usually were assisted with vascular surgeon. Vascular surgeon could be helpful “tool” during procedures of patients with higher risk of vascular complications, significant arteriosclerotic disease, intra-operative technical complications, thrombotic complications or could be helpful with diagnostic prior to surgery or vascular complications following transplant as well treatment such PTA as more common procedures in vascular specialty.

The Gift of Life and Nonadherence in Renal Transplant Recipients

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The gift of life metaphor is pervasive in discourses related to the donation of body tissues. Despite the ubiquitous nature of the metaphor, it has been absent in key contexts and issues that occur post-transplant, such as high instances of non-adherent (NA) behavior expressed by renal transplant recipients. The underrepresentation of issues such as NA in the extant literature has been acknowledged by researchers. This paper investigates the gift of life discourse through the lens of NA among renal transplant recipients, focusing on the central question: How does the gift of life discourse in live donation awareness and education influence nonadherent behavior among renal transplant recipients? Using critical discourse analysis, this paper assesses a breadth of publicly available living donor awareness and education texts, including donor and recipient testimonial videos, images/other written texts (e.g., transplant process guides, live donor outreach letter templates, posters, etc.) circulated from institutions and figures of authority in the Canadian healthcare system. Texts were selected based on content containing symbolism and meanings associated with the gift of life metaphor, and where live kidney donation information was included. The data were analyzed for content line-by-line, ideas and concepts were hand-coded iteratively with emerging concepts classified along themes of morality, giving, receiving, and reciprocating. The gift of life, synonymous with altruistic morality, was shown to dialogically enable donors and recipients in their respective obligations to give and to receive. However, the language of the gift of life is noticeably absent when it comes to repaying; thus, diminishing the duty of recipients to care for their donated organ and potentially influencing patient NA behaviors. This fissure in the gift of life rhetoric offers a fresh perspective that may provide insight into why issues of medication NA is plaguing the transplant community. Postig the gift of life metaphor into notions of reciprocity found in live kidney donation education and awareness texts move towards balancing the moral asymmetry across giving and receiving, and repaying, that is conjured within transplant discourse. This study provides a nuanced understanding of the gift of life discourse within the context of live kidney donation. The ways in which the donor and recipient are discursively positioned within live kidney transplant texts serve to simultaneously magnify and undermine notions of reciprocity. Further, the symbolic meanings associated with the gift of life are replaced by biomedical language in the post-transplant context (i.e. when the giving and receiving have been completed), leaving the recipient constrained when reconciling conflicting feelings of guilt and gratitude around the impulse to repay by avoiding NA behaviors. This observation provides a possible explanation for the high instances of NA among renal transplant recipients.
Non-melanoma Skin Cancer With an Aggressive Course in Kidney Transplant Patients Treated With Rapamycin

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Introduction: Non-melanoma skin cancer (NMSC) represents the most frequent malignancy in patients with solid organ transplantation, with a high risk of metastasis (MTS) and death related to factors such as chronic immunosuppression, exposure to ultraviolet (UV) radiation, and HPV infections.

Objectives:
- To describe the features of non-melanoma skin cancer (NMSC).
- To highlight the need for dermatological control in order to assess risk factors, precancerous lesions and make an early diagnosis.

Materials and methods: We present three renal transplant patients assisted by Dermatology at the Renal Transplant Unit of CRAI Sur, Hospital Intezional General de Agudos "Gral. San Martin", La Plata, Argentina. Patients with multiple lesions under treatment with rapamycin and aggressive evolution were chosen. Risk factors related to the multiplicity and dismal evolution of NCC (signs of photodamage, preneoplastic lesions, history of NCC) were evaluated prior to evaluation at the unit; we also analysed age of presentation, sex, transplantation timing, initial immunosuppressive regimen and subsequent modifications, type of NMSC, treatment and evolution.


Conclusions:
1- The NMSC in these patients presented with multiple lesions and clinical and histological characteristics related to an aggressive course (MTS and death in two cases).
2- Immunosuppressive therapy with rapamycin did not modify the outcome and development of multiple lesions despite its known antiproliferative and angiogenesis effects.
3- All our patients were men and presented risk factors for NMSC (photodamage, actinic keratoses, more than five years post-transplantation, history of prior NMSC, induction and immunosuppressive therapy).
4- Dermatological control is crucial in order to identify risk factors, promote photoeducation and make a prompt diagnosis.

Molluscum Contagiosums as a Cutaneous Marker of Immune Reconstitution Syndrome in a Renal Transplant Patient

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Introduction: Immune reconstitution inflammatory syndrome (IRIS) is an important complication after initiation of antiretroviral therapy associated with considerable morbidity and mortality in HIV patients, but has been rarely reported in solid organ transplant patients. IRIS is a host response resulting in paradoxical worsening of an infectious disease which occurs after reversal of an immunosuppressed state. Although a working paradigm of the pathophysiology of IRIS occurring in the posttransplant setting has not been established, current evidence suggests an imbalance between pathogen directed host inflammatory (Th1, Th17) and anti-inflammatory (Th-2, Tregs) effector cells resulting in hyperinflammatory response to a pathogen with ensuing tissue damage.

Objectives: To describe a case of IRIS in a renal transplant patient with molluscum contagiosum highlighting the difficulty in differential diagnoses and the importance of early detection.

Case report: A 41 year-old male patient with accelerated hypertension received a cadaveric graft on October 2012. IS: Tacrolimus Mycophenolate Mofetil and steroids. On October 2015 he presented seizures with ischemic lesions in MRI whith normal CSF and deep vein thrombosis in leg for which he began anticoagulation. Consulted in January 2021 for hiporexia with marked weight loss, diarrhea and fever, presenting severe gingival hyperplasia with loss of teeth of months of evolution and cutaneous umbilical papular lesions in neck, face and limbs. Laboratory: creat 1.7 mg/dl, WBC 3100, Htc 28, platelets and hepatic enzimes normal, COVID PCR, Cryptococcal antigene and CMV PCR negative, parvovirus, HIV, VDRL, HBV and HCV negative. Tacrolimus was stopped (dosages of 19ng/ml) remaining with hydrocortisone 100mg every 8 hours. Control at 24 hs: WBC 1900 with 55 % NTF, Htc 28 Platelets 178000; colony stimulation factor and Ganciclovir were indicated. Chest CT: emphysema without infiltrates. Biopsy of oral lesions compatible with gingival hyperplasia due to drugs, probably secondary to tacrolimus. Biopsy of limb lesions: molluscum contagiosum. Tacrolimus was switched to rapamycin, and he continued with steroids. On the 16 th day he was readmitted due to exacerbation of skin lesions and fever, coinciding with an increase in CD4 and improvement of blood analysis. The picture was interpreted as IRIS, increasing doses of steroids to 20mg/day, improving the picture until healing of skin lesions.

Conclusions: Our study highlights the clinical relevance of recognising IRIS in patients transplanted with solid organs through the exacerbation of skin lesions.
Factors Contributing to Acute Rejection Within One Year of Kidney Transplantation With a Perspective of Tacrolimus Trough Level; A Nationwide Cohort Study

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Introduction: Rejection after kidney transplantation (KT) is an important cause of poor long-term survival of the graft. Tacrolimus (TAC) is one of the most critical medications of immunosuppressants in KT, and maintaining the proper blood concentration is essential to prevent acute rejection and toxicity of immunosuppressants. We analyzed the risk factors for acute rejection within one year of KT with a perspective of TAC trough level in a nationwide cohort study.

Method: Data of 4,153 KTUs using the database of Korea Organ Transplantation Registry (KOTRY) were retrospectively analyzed between April 2014 and December 2020. Clinical information, including TAC trough level and graft function, was reviewed in donors and recipients. Risk factors were analyzed for biopsy-proven acute rejection (BPAR) with a t-test and chi-square. In subgroup analysis, the risk of BPAR was analyzed again by dividing the TAC trough level at discharge into the higher and lower group.

Result: There was no statistical difference in characteristics of donors and recipients between the BPAR group and no BPAR, including the immunologic factors, such as HLA mismatching, pre-existing donor-specific antibodies. In subgroup analysis between lower TAC trough level (<5ng/mL) and higher TAC (≥9ng/mL) at discharge, there was somewhat increased BPAR in lower TAC without statistical significance (10.7% vs. 8.9%, P=0.137). Renal functions after KT were better in the no BPAR group with statistical significance (p<0.001).

Conclusion: Lower tacrolimus trough level at discharge tends to be associated with a risk of acute rejection within one year of KT. Extensive data and well-designed studies are needed to further investigate tacrolimus level as a risk factor for acute rejection.

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Modern Medicine Needs Modern Technology Tools

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Introduction: Early detection of subclinical rejection is critical to prevent the allograft loss. Currently used methods to detect subclinical rejection include surveillance biopsy protocol, serum creatinine level, eGFR or DSA; however, these methods have limited sensitivity and specificity to accurately detect subclinical rejection. Donor derived cell-free DNA (dd cf-DNA) is a non-invasive biomarker for allograft injury and has been shown to predict allograft rejection with higher sensitivity to detect subclinical rejection compare to some methods (1,2). Here, we show the value of dd cf-DNA in detecting early allograft rejection by presenting two cases where dd cf-DNA assay, AlloSure (CareDx) detected subclinical rejection while other indicators showed stable allograft function.

Methods: Ochsner uses AlloSure (CareDx) for a surveillance for the high-risk patients.

Results: Thirty-two years old Caucasian female with end stage kidney disease secondary to HIV infection underwent deceased-donor renal transplant in 2018 with KDP1 19% and cPRA 84%. Serum creatinine level had been stable at 1.1mg/dL to 1.2mg/dL post-transplant. This patient was monitored using AlloSure (CareDx) for 1-, 2-, 3-, 4-, 6- and 9-month post-transplant. AlloSure values for month 1 to 6 were 0.21, which indicates stable allograft function. However, at 9-month post-transplant, AlloSure value went up to 4.5%, which indicates possible allograft injury, while serum creatinine level remained stable at 1.2mg/dL with low level of class 2 DSA (DR-1573). Despite stable creatinine level and low level DSA, we initiated biopsy because of sharp increase in AlloSure value. Biopsy revealed acute T-cell mediated rejection and acute vascular rejection. The second case is a 33 years-old Caucasian female with history of previous renal transplant. The first allograft failed in 2018 due to renal artery and vein thrombosis. The patient underwent deceased donor kidney transplant in 2019. Serum creatinine level was stable at 1.0 – 1.3mg/dL and sharp increase in respectively. At month 3, AlloSure value went up to 0.78% but DSA was negative. We initiated biopsy based on increase in AlloSure value and it revealed acute antibody mediated rejection (ABMR) (DR-1573). For all 3 cases, biopsy would not have been initiated most likely due to stable creatinine level and weak or negative DSA. If this had gone untreated for long period of time, this would have led to significant decrease in graft survival. These cases demonstrate that normal serum creatinine does not mean patient has no active inflammatory process. When other indicators are normal/stable, AlloSure was able to detect early rejection. All three cases demonstrated the value of AlloSure as a monitoring tool for detection of early allograft rejection.
Introduction: Laparoscopic surgery and currently robot-assisted surgery have transformed the current surgery paradigm, showing a lower systemic inflammatory response, less post-operative pain, smaller incisions, shorter hospital stay and better cosmesis. Recipients of a kidney transplant in which the approach of choice is conventional surgery with retroperitoneal access, either due to their comorbidities, the size of the incision or their immunosuppression, present risk factors for surgical wound complications. Laparoscopic kidney transplantation allows our recipients to access the benefits of minimally invasive techniques, which have been offered to donors for a long time. Since its publication by Rosales et al and Modi et al, this technique was displaced with the spread of robotic surgical systems. However, their high costs make them inaccessible to the health systems of developing countries. For this reason, we set out to retake the lost art of laparoscopic transplantation. Our purpose is to show the first laparoscopic kidney transplantation in Argentina and its results.

Methods: Donor: deceased donor, male, KDPI 5%, cold ischemia time 14 hrs, left kidney, 2 arteries. Recipient: females, 54 yrs old, bmi 27.8, membranous glomerulopathy, 6 yrs on hemodialysis. Surgical technique: transperitoneal approach, the surgical steps are resumed in figure 1. We used modifications of Modi’s technique: different incision (midline instead of pfannestiel approach), use of ureteral stent, and cold jacket gauze for local hypothermia.

Results: - Perioperative results surgical time: 187 minutes. Vascular anastomosis time: 39.5 minutes and the urological time was 35 minutes. The cold ischemia time of the graft was 14 hrs. The blood loss was 280 cc.
- Post-operative evolution The patient progressed favorably in the immediate postoperative period, with early graft function and a progressive decrease in urea and serum creatinine values without registering any medical or surgical complications. She did not require hemodialysis during hospitalization. She continued with her maintenance immunosuppression scheme, receiving discharge on the 5th post-operative day. 1 month post op Creatinine was of 1.1mg/dl. 6 month Creat 1.2 mg. No rejections were detected at 6 month follow up

Conclusions: Laparoscopic kidney transplantation is a complex technique that requires previous experience in transplant and laparoscopic surgery. It is a valid option for minimally invasive surgery in recipients with good results in trained teams and with costs that non developed countries health system can afford.

References:
**Abstracts**

**P8.047**

**An Arrow for Two Targets: Kidney Donation in Unilateral Renal Artery Stenosis**

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**Background:** Chronic Kidney Disease (CKD) is getting more and more common in society and at the same time availability of donors is very sparse. In a resource limited country like India, where the cadaver donation rate is low and people don’t readily agree for live donation to their own family members, we have to choose between the optimal and only donors available, even though marginal.

**Methods:** This is a case report of 23 yrs old male patient, a case of IgA nephropathy with CKD on hemodialysis since one month. He was under the transplant workup with mother as donor but unfortunately mother’s glomerular filtration rate in DTPA scan was low despite a creatinine of 0.8mg/dl, so mother was cancelled as donor. Patient was left with one donor only, his father who was hypertensive since five years. On further investigation father had right renal artery stenosis at osteum, but glomerular filtration rate and other reports were within normal limits. We did a right open donor nephrectomy and transplanted right kidney in the recipient. Right renal artery ligation was done distal to the ostial stenosis.

**Results:** The transplant surgery was uneventful and the recipient attained a creatinine of 0.9mg/dl on 5th postoperative day. Donor was discharged on 3rd day with a creatinine of 0.8mg/dl. Donor had a normal blood pressure postoperatively and didn’t require any hypertensive medications till date.

**Conclusion:** A person with unilateral renal artery stenosis can be taken as donor if other optimal donors are not available. It will have two advantages, not only the recipient is cured of the disease but also the donor is free from hypertension or from any risk of development of hypertension in future.

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**P8.048**

**Organ Preserving Cardiopulmonary Resuscitation in A Resource Limited Country to Increase Donor Pool**

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**Background:** In developing nation where modern advances in deceased donation is far from reach, cost effective procedures like organ preserving cardiopulmonary resuscitation (OPCPR) can result in considerable expansion of donor pool.

**Methods:** A retrospective analysis from a single center of India. The outcome measured was difference in OPCPR compared to standard criteria donor (SCD) in censored patient and graft survival through Kaplan Meier analysis. The secondary outcomes were surgical, rejection, and infectious complications.

**Results:** We report our experience of increasing donor pool by OPCPR by 35%. Patient survival was similar in OPCPR group compared to SCD (85.7% vs 95.1%; p-value = 0.19). Graft survival was similar in both groups (96.4% vs 95.1%; p-value = 0.85). The patient survival was similar in non-AKI (acute kidney injury) OPCPR compared to AKI OPCPR (85.7% vs 77.8%; p-value = 0.49). The graft survival was similar in both the groups (85.8% vs 92.9%; p-value = 0.70). The secondary outcomes measured were also similar.

**Conclusion:** Our preliminary report shows acceptable outcomes in OPCPR donors. Hence, we encourage OPCPR worldwide in an effort to further increase the donor pool. This report will be a learning tool to replicate in other resource limited nations.
Background and Aims: Chronic active antibody-mediated rejection (cAAMR) is one of the main causes of late allograft failure after kidney transplantation. Data on the management of chronic active antibody-mediated rejection after kidney transplantation are limited. Intravenous immunoglobulin (IVIg) is one of the treatment options known to have powerful and multiple immunomodulatory effects. High-dose IVIg delivers a lasting immunomodulatory effect on T cells and especially B cells, resulting in changes in the induction of B cell apoptosis and downstream modulation of B cell signaling.

Methods: This was a single-center study of kidney transplant recipients (n=10) treated with high-dose intravenous immunoglobulin for biopsy-confirmed cAAMR. IVIg infusions (1 g/kg) were performed every 4 weeks for 6 months. All patients were followed for at least 12 months clinically and by laboratory tests for graft and patient outcomes.

Results: Mean age of recruited patients was 47.3 ±12.74 years. Most of them had first kidney transplant. Glomerulonephritis represented the most common cause of end-stage kidney disease. The time frame for cAAMR development was 32 [7;60] month. 2 patients died from coronavirus COVID-19 and 4 (40%) patients started dialysis during the follow-up period. 4 (40%) kidney transplant recipients with functioning grafts had no significant changes in serum creatinine, glomerular filtration rate and proteinuria after treatment.

Conclusion: Monotherapy with intravenous immunoglobulin seems not to be an effective treatment strategy for chronic active antibody-mediated rejection of kidney transplant. New therapeutic approaches are needed to improve the outcome of cAAMR.
P8.050
Pediatric Donor Transplants to Adult Recipients: Follow-up And Outcome

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Introduction: The use of kidneys from pediatric donors, neonates in adults, is an option considered possible in teams dedicated to kidney transplantation. We present our experience with transplantation of separately kidneys from neonatal donors implanted in adult recipients.

Patients: Four adult patients aged 25 to 35 years were transplanted with kidneys from neonatal donors, less than 1 year old, with the usual technique. They received immunosuppression with Cyclosporine, Azathioprine and Prednisone.

Results: During the first 15 days it was necessary to practice hemodialysis. From then on, the renal function of the graft improved until plasma creatinine of 1.7±0.5 mg/dl was reached. From the first 3 - 4 weeks the graft reached the size of an adult kidney, controlled by ultrasound. These patients, after 25 years, keep the graft functioning, with plasma creatinine less than 1 mg/dl. They do not have high blood pressure and have not had acute rejection.

Conclusion: Kidneys from child donors can be grafted in isolation with excellent results. Only technical-surgical reasons can prevent the use of organs from donors under 1 year of age. The result in our hands with this type of donor shows us that it is possible to use it.

P8.051
Corticosteroids Withdrawal in Renal Grafted Patients: Follow-up and Outcome

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Introduction: Steroids are powerful antiinflammatory with immunosuppressant effects utilized in maintenance therapy following kidney transplantation and are associated with a higher rate of side events in comparison with protocols involving early corticosteroid withdrawal. The present paper reports the results of cessation of steroids in stable maintenance renal transplant patients.

Patients and methods: One hundred sixty seven deceased kidney grafted patients (54% men), aged 57.5±12.4 years, with follow-up of 84 months and steroids withdrawal period of 60 months (1-198) follow-up steroid free were studied. Etiology of end stage renal disease was secondarily to Glomerulonephritis 31%, Diabetes 22%, Polycystic disease 14%, Tubulointerstitial nephropathy 13%, Vascular 5%, Unknown 17%. The patients were on Prednisone 5-10 mg daily combined with Cyclosporine 50-150 mg/Tacrolimus 0.5-6 mg, associate to Mycophenolate Mophetyl 250-2.000 mg, Sodium Micophenolate, 360-900 mg or Azatioprine 50-75 mg, and Everolimus 1-4 mg. Steroids were diminished gradually in three months period and some patients receive monotherapy only.

Results: Basal serum creatinine was 1.54±0.6 mg/dl and after five years follow-up 1.4±0.5 mg/dl. Basal blood glucose concentration was 130±12 mg/dl and after five years 109±0.8 mg/dl. Weight was maintained. At 5 years, graft and patient survival were 100%. There was no acute rejection after steroids withdrawal. After withdraw blood pressure control was achieved with less antihypertensive drugs. Lipids diminished slightly with less cholesterol-lowering drugs.

Conclusion: Corticosteroids could be withdrawn safely in stable renal transplant patients and avoid morbidity and adverse events related to chronic utilization improving survival and quality of life.
Long-term Outcomes and Predictors of Graft Function in Living-Donor Preemptive Kidney Transplants

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Background: Beyond the new strategies for dialysis treatment, kidney transplantation has already been associated with better outcomes for patients with advanced kidney chronic disease (CKD), and a preemptive kidney transplant seems to be the preferred option for those patients. Thus, this study purposed to evaluate predictors of long-term graft function and unfavorable outcomes in living-donor preemptive kidney transplant recipients.

Methods: Single-center cohort study enrolled 222 living-donor preemptive kidney transplant recipients transplanted between 2011 and 2016 and followed up to 2021. Five-year graft function was estimated by CKD-Epi (5-year-eGFR). The primary outcome was composed of death, graft loss, acute rejection, and 5-year-eGFR < 30 mL/min/1.73m2. The multivariable analysis for 5-year-eGFR was performed by linear regression and logistic regression for the primary outcome.

Results: Recipients were 40 (31; 48) years old, 59.9% were male, and 35.1% had CKD due to chronic glomerulonephritis. Donors were 48.5 (41.0; 55.2) years old, being most frequently siblings (50%) or parents (28.3%). One-third of patients received ATG as an induction strategy (30.2%), followed by Tacrolimus + azathioprine (59.5%) or cyclosporin + azathioprine (14.4%) or tacrolimus + mycophenolate (11.3%) as the maintenance immunosuppression. The overall incidence of acute rejection, graft loss, and death was 20.3%, 6.3%, and 0.5%, respectively. The median follow-up time was 89.9 months, and the median 5-year-eGFR was 54.7 mL/min. Sixty-five patients presented the primary outcome (29.2%), significantly associated with HLA compatibility, not using induction therapy and CMV-related rejection. Compared with identical HLA matches, the OR was 6.81 for haploidentical (P=0.001) and 11.2 for distinct (P<0.001) HLA matches. In addition, the probability for the primary outcome was reduced by 81% (OR=0.19, p<0.001) for patients who received ATG as induction therapy and 4-fold higher in those who had CMV-related events (OR=4.09; p=0.001). In the linear regression, the association with 5-year-eGFR was less evident with HLA matches and AR than donor age. Thus, the identical HLA (B=+6.04; p=0.09) match and AR (B=−6.34; p=0.07) tend to be associated with 5-year-eGFR in the linear regression, while donor age (B=+0.69 per year old; p<0.001) presented a significant and inverse association.

Conclusion: In recipients of living-donor preemptive kidney transplants, the HLA matches, thymoglobulin induction therapy, and CMV-related events were predictors of composite outcomes of long-term death, graft loss, acute rejection, and low grade of graft function. In addition, only donor age was independently associated with long-term graft function.

Case Report: Nephrotic-Range Proteinuria in a Deceased Donor Recipient With Acute Antibody Mediated Rejection And Familiar FSGS

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A 47yo female patient presented early after transplant a nephrotic-range proteinuria despite treatment for active antibody mediated rejection (AMR). She had undergone a deceased donor kidney transplantation after a desensitization protocol with immunoglobulin for HLA antibodies; immunosuppression consisted of 6mg/kg thymoglobulin for induction and triple therapy (mycophenolate, tacrolimus, prednisone) for maintenance. She was previously diagnosed with familiar focal and segmental glomerulosclerosis (FSGS) due to a IVS9 + 5G>A mutation of the WT1 gene; her clinical history was characterized by corticosteroids resistant nephrotic syndrome and arterial hypertension that evolved to anuric end-stage kidney disease and 16y of hemodialysis treatment. Her daughter was also affected by FSGS related to WT1 mutation. The caucasian female donor of standard criteria had known systemic hypertension and final creatinine of 0.89mg/dl; previous A68 donor-specific antibody (DSA) was absent at Tx. Graft dysfunction and a macro-proteinuria were present since the first week. Day 10 graft biopsy displayed AMR features and C3 mesangial deposition; resurgence of A68 DSA and positive flow-cytometry crossmatch confirmed AMR which was treated with pulse corticosteroid, plasmapheresis, human immunoglobulin and rituximab. A second biopsy revealed collapsing glomerulopathy with C3 deposition, C4d negative, and minimal microvascular inflammation. Because the early FSGS features should not be the recurrence of the familiar FSGS nor come from the rejection episode, a donor cause was pursued. The other kidney recipient from the same donor also developed early proteinuria and graft dysfunction, but no rejection. Sanger sequencing of donor APOL1 gene revealed G1/G2 risk alleles. Final diagnosis was APOL1 nephropathy (collapsing glom.) from the donor with superimposed AMR. This case illustrates the unexpected proteinuria from the initial diagnosis of rejection and familiar FSGS.
P8.054

Out of the Box. Immunosuppressive Therapy With Four Drugs As Rescue Therapy in Kidney Transplant Recipients With Chronic Allograft Rejection

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Introduction: Persistent or repeated episodes of acute rejection (AR) may lead to chronic allograft damage. Antibody-mediated rejection (AMR); T-cell mediated rejection (TCMR) and mixed variants (MR) of chronic kidney allograft rejection (CR) are nowadays considered as the main causes of graft loss (GL). This encompasses from endothelial damage up to fibrosis challenging immunosuppressive therapy (IT) management. IT reinforcement with a four-drug scheme (4D) including m-TOR inhibitors, anticalcineurinics, mycophenolate and steroids, could be a good strategy in this scenario, nevertheless there is no consensus about it. We present our experience with 4D in kidney transplant recipients (KT) That presented with CR or recurrent episodes of AR.

Objectives: To evaluate kidney graft function (KGF), incidence of rejection and safety of a 4D in KT with CR or recurrent episodes of AR.

Methods: KT on treatment with 4D from 2008 to 2021 were included. KGF was evaluated by estimated glomerular filtration rate with CKD-EPI (eGFR) and urinary protein/creatinine ratio (PCR) at 3, 6 and 12 months. Kidney biopsies and panel reactive antibodies (PRA) by Luminex were performed before and after introduction of 4D. BK virus (BKV) incidence, infectious (IE) and neoplastic (NE) events were recorded during the follow up.

Results: 16 KT (median age 45 ± 11 years) were treated with 4D during 52.8 (17-106) months. 43.8% of them were women, 50% were deceased KT. The median post transplant time was 108 (60-129) months. Reasons for 4D introduction were CR in 87.4% of the cases (MR 50%; TCMR 31.3%; AMR 6.3%) and in the remaining 12.6%, recurrent or persistent acute TCMR. Median eGFR was 42 (27-66); 44 (31-62); 48 (33-60) and 48 (32-65) ml/min prior to IT change, at 3, 6 and 12 months respectively. At baseline, mean PCR was 179 (147-664) mg/g without significant changes during follow up. Biopsy proven AR was found in 37% of KT under 4D. No NE were registered. 43% of the patients presented a non major IE, and only one patient was BKV positive during follow up with 4D. There was one GL, one loss of follow up and one death due to sepsis with functioning graft.

Conclusions: KT patients with CR or recurrent episodes of AR changed to 4D IT stabilized their renal function and proteinuria. The incidence of new biopsy proven AR was 37%, and no new DSA were found or serious adverse events reported during follow-up. 4D could be a good option to halt the progression of renal damage due to rejection in KT.

P8.055

Systemic Heparinization in Kidney Donors During Nephrectomy

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Introduction: Thrombotic complications on the graft are the most terrifying situations in living donor transplantation. Yet, up to this moment no clinical guidelines assure that the use of heparin during surgery prevents from the appearance of those events. Our hypothesis is that during surgery, there is a significant venous ectasia that may increase the risk of vascular thrombosis.

Methods: We conduct a retrospective trial to asses whether the use of heparin during laparoscopic donor nephrectomy causes surgical complications on the donor as well as the recipient. We select two groups, A (with the use of 7500 units of sodic heparin before vascular clamping) and B (without heparin).

Results: From may 2015 up to may 2021, fifty living laparoscopic transperitoneal donor nephrectomies were performed at our Institution. Of them, 68% were females and 32 % males ranging from 27 to 72 years old. Specifically, 7 cases with multiple renal arteries and 3 cases with retro-aortic renal veins. All surgeries were performed by one surgeon with a pure laparoscopic transperitoneal approach. We use heparin in 35 patients (Group A-70%), the control group B, represents the 30%. We did not find any differences in terms of surgical complications on the donor, graft and recipient survival. However, delayed graft function was higher in the group without heparin, 5 cases that represents 30% in group B, in contrast with A that with no patient. With a median follow up of 20 months graft and recipient survival is 96%.

Conclusion: Considering the aforementioned data, the use of heparin before clamping the renal vessels, have no detrimental effect on the postoperative curse of both patients. Hypothetically, this approach may reduce the risk of suffering from vascular thrombus complications on the graft. Future randomized prospective clinical trials would eventually define the real role of this line of action.
P8.056

Laparoscopic Managment of Ureteral Stricture After Kidney Transplantation

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Introduction: The development of ureteral strictures arises as one of the most challenging scenarios for transplant surgeons. Different strategies, from open reconstructive surgeries to minimally invasive approaches, may cope with this situation. In this study, we particularly want to clarify the role of laparoscopy.

Method: We present the case of a 45 years old female, who had a kidney transplant surgery 15 years ago. During its regular check up, their clinician found a hydrenephrosis of the graft that affected their kidney function. First, a nephrostomy tube was inserted to prevent further damage and also to perform a pielography. A 2 cm ureteral stenosis prior to the ureterovesical junction was diagnosed. Therefore, we offer a laparoscopic reconstructive surgery.

Results: A four-ports transperitoneal approach was attempted. At the beginning, the ureter was dissected from cranial to caudal on its half lower portion. Then, bladder was release to gain flexibility. After a ureteral catheter was inserted from a lower lap port, an intravesical ureterovesical anastomosis similar to the Leadbetter technique was performed. Patient undergo a posoperative time without complications. At the moment, graft function is optimal.

Conclusion: We definitely believe that there is a window to increase the use of laparoscopy in the management of ureteral strictures in renal allografts. A sharply determination of patient and disease characteristics is mandatory to improve posoperative results. Undoubtedly, patient outcomes are strictly related to the experience in minimally invasive approaches.

P8.057

Cannabidiol (CBD) Oil and Tacrolimus: The Unexpected High in Renal Transplant Recipients – Case Series and Review

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Introduction: Calcineurin inhibitor (CNI) based regimens afford the greatest protection against acute rejection and are used in > 90% of kidney transplant recipients. Cannabidiol (CBD) has been advertised as a natural remedy to treat several disorders. Information on the concurrent use of CBD and tacrolimus is limited. Herein we describe four cases of patients reporting CBD use post kidney transplant, and the effects on tacrolimus drug levels.

Results:

Case 1: 38-year-old male with chronic kidney disease secondary to polycystic kidney disease (PKD) received a living unrelated kidney transplant from his spouse. His course was uncomplicated until 3 months post-transplant when he started using CBD oil for sleep. One week after starting CBD oil he presented for follow up and was noted to have a tacrolimus level of 40.1 ng/mL. His tacrolimus level returned at 20 ng/mL after stopping CBD oil.

Case 2: A 55-year-old male with chronic kidney disease secondary to lithium toxicity received a living unrelated kidney transplant. He self-started CBD oil three weeks post-transplant and was noted to have an increase in tacrolimus level to 16.1 ng/mL. He elected to stop his CBD oil because he thought it may be interfering with his medications and four days later his tacrolimus levels decreased to 8.8 ng/mL.

Case 3: 46 year old male with ESRD ascribed to diabetes mellitus received a deceased donor kidney transplant. One year later he presented for a routine follow up and was noticed to have a tacrolimus level of 2.4 ng/mL. He reported taking CBD oil for the past 6 weeks for anxiety. His tacrolimus was increased, and he underwent a kidney transplant biopsy which showed acute cell mediated and vascular rejection with chronic active antibody mediated rejection. HLA testing showed de novo HLA antibodies to DQ7 and DQA1*05.

Case 4: 64 year old female received her pancreas transplant in 2005. 14 years later patient presented for a routine follow up and was noticed to have a tacrolimus level of 12.1 while on a steady dose of 1 mg BID. She endorsed starting CBD oil a month prior for relief of her neuropathy symptoms. Her tacrolimus was adjusted down to 0.5 mg BID with improvement in her level to 7.

Discussion: Cannabidiol (CBD) is a non-psychogenic cannabinoid found in the Cannabis sativa plant. The Agriculture Improvement Act of 2018 legalized production of industrial hemp plants, so long as it contained no more than 0.3% of delta-9-tetrahydrocannabinol (THC). Interestingly, amongst our cases 3 resulted in an increase in tacrolimus levels and another resulted in a marked decrease in tacrolimus levels which precipitated allograft rejection. All cases of increased levels occurred without a change in tacrolimus dosing and relatively stable levels prior to known administration. Tacrolimus levels improved after stopping CBD oil supplements. The solitary case of reduced tacrolimus levels following CBD oil exposure may have been related to another compound within the CBD oil labelled product.
Second and Third Renal Transplant During COVID 19 – A Single Center Experience in India

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Background and Aims: Covid first wave caused thousands of CKD patients a great ordeal in India as the nationwide lockdown and stoppage of planned transplant operations continued till the month of June 2020. The covid infection was very severe in CKD patients: much so in patients with failed grafts. As the unlocking process started the transplant programs were also initiated in our institute. This study was done to know how covid-19 had affected the outcome and our understanding of renal transplantation in high-risk recipients.

Method: Total 20 cases of 2nd and 3 cases of 3rd renal transplant and 9 cases of HLA sensitized transplantation were done from June 2020 to October 2021. All had living donors. They were monitored for a period of up to 17 months post-transplant.

Results: 26 patients (81.25%) underwent HLA desensitisation according to our hospital protocol. Among the 32 cases 13 (40.6%) had history of covid infection prior to the transplant, 2 of them had severe lung fibrosis requiring prolonged (>2 months) inhalational oxygen post recovery from covid. Only 9 (28.12%) recipients were completely vaccinated against covid-19 prior to their transplantation although all received it by the end of observation period. Graft biopsy done in 16 recipients during observation period revealed ATN in 8 cases, ACR in 3 cases, ABMR in 1 case each of TMA and ascending pyelonephritis were seen. The average duration of follow-up was of 5.6 months and average mean creatinine at discharge was 1.89. Among the 32 patients we lost 6 (18.75%), all due to severe forms of infection (fungal endocarditis-1, Guillain-Barre syndrome-1, mucormycosis-1, severe re-infection with covid-19 - 2, sepsis - 1). Incidence of acute gastroenteritis and urinary tract infection was more than our normal institutional average but the patients had lower incidence of respiratory tract infections. Post transplantation 7 (21.8%) had acquired covid 19 infections among them 2 died at 1 month and 6 months post transplantation respectively, rest all recovered uneventfully. Those who died with covid-19 had the infection twice, both before and after transplantation with a gap of more than 9 months and had received 2 doses of vaccination. Infectious complications were seen more in desensitized patients as expected.

Conclusion: In conclusion transplantation done during covid-19 pandemic and in covid-19 recovered cases were challenging. The pandemic uncovered some rare infections which demanded more attention not only from the nephrologists also from anesthesis, pulmonology and infectious disease physicians. Although this pandemic had a great impact on the whole system, with time our understanding of the covid-19 infection has improved for better.
Renal Transplantation in the Elderly. Are They All the Same? A Multicenter, Comorbidity Based Study

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Background: The age for renal transplantation (RT) is no longer a limitation and several studies have shown benefits in the survival of elderly patients. The aim of this study was first, to examine the relationship of the baseline Charlson comorbidity index (CCI) score to morbid and mortality after transplantation, and second to identify other variables affecting patient and graft survival.

Methods: In this multicentric observational retrospective cohort study, we included patients older than 60 years admitted on the waiting list (WL) for deceased donor RT from 01/01/2006 until 31/12/2016 in the eight participating centers. The CCI score was calculated for each patient at inclusion on the WL.

Results: Data for analysis was available of 387 patients. Mean age was 68±6.2 years, 60% were males. The patients were divided in tertiles of CCI: group 1(CCI:1-2) n=117, group 2 (CCI: 3-4) n=158 and group 3(CCI: ≥5) n=112. Median time on dialysis before RT was 51(29-73) months. Median follow up time after RT were 53 (16-85) months. Median CCI score for the whole cohort was 3 (2-5). The number of infectious disease re-admissions were higher along the CCI groups. The number of surgical complications were significantly higher in CCI group 3 (30.4 %), p< 0.013. Acute rejection (AR) was less frequent in patients with high CCI score compared to group 1 (p<0.013). Survival of patients with functioning graft was significantly different between CCI groups at 1, 3 and 5 years respectively: 90%, 88% and 84% for group 1, 88% and 72% for group 2, and 87%, 75% and 63% for group 3. Log Rank test: 15.660, P< 0.0001. Variables significantly associated with mortality were: CCI score [OR=1.73 (IC 1.392-2.169), p=0.0001], Delayed graft function (DGF) [OR=0.14 (IC 0.005-0.477), p=0.001], HLA mismatch [OR=1.39 (IC=1.059-1.849), p=0.018], length of hospital stay [OR=1.04 (IC 1.022-1.058) p=0.0001], surgical complications [OR=5.87 (IC 1.737-17.462), p=0.004], and creatinine at 5 years [OR=1.30 (IC 1.095-1.547) p=0.003]. Death censored graft survival was not different between the 3 CCI groups. Variables significantly associated with graft loss were: AR [OR=8.06 (IC 1.305-49.807), p=0.025], creatinine at 3 years [OR=7.06 (IC 2.863-17.443), p=0.0001] and proteinuria at 3 years [OR=1.00 (IC 1.001-1.003), p=0.004].

Conclusions: Individualized strategies to modify these variables may improve patient’s morbidity and mortality after RT.
P8.062

Prevalence of Hyperkalemia (HK) Among Stable Kidney Transplant Patients

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Objectives: To determine the characteristics of renal transplant patients with hyperkalemia. Evaluate the use of Renin Angiotensin Aldosterone System inhibitors (RAASi) in this population.

Materials and Methods: Laboratory records of kidney transplant patients in our unit between January and December 2021 were evaluated. Clinical variables (age, time since transplant, sex, use of RAASi) and laboratory variables (kalemia, creatininemia, proteinuria) were analyzed.). Renal function was calculated using the CKD EPI formula. Only records of patients in stable conditions were considered, discarding those records during hospitalizations or clinical complications. Two groups were divided with and without records of hyperkalemia (greater than or equal to 5 mEq/l) and statistical differences between groups. A value of p <0.01 was considered significant.

Results: In the evaluated period, out of 454 patients under follow-up, 438 had a record of potassium values obtained in the database, to which a total of 1349 determinations were made. Of these determinations, 138 had high values (10.23%), which corresponded to 74 patients (16.3% of the study population). Of these 74 patients, 29 (39%) had more than one elevated record. Results are resented in Figure 1. Patients with hyperkalemia presented higher creatinine values, lower glomerular filtration rate and lower red series values. The group with hyperkalemia had a significantly greater use of RAASi, mainly due to the use of Angiotensin Converting Enzyme Inhibitors (ACEi). No differences were observed between both groups regarding the use of low doses of ACEi/ARB (Angiotensin Receptor blockers). The results are shown in Figure 1. The frequency of hyperkalemia was significantly higher in the group with renal stage IV (39.34%) vs stage I-II (2.68%) of chronic kidney disease. In stages I-II of CKD, 40% of patients (60/149) are found with RAASi, while in stage IV it rises to 60% (37/61; p 0.007). About 29% of patients with RAASi in both groups were on low doses of the same.

Conclusions: 16% of transplant patients presented hyperkalemia in our series, with a significant difference between those with early stages of kidney disease (2.68% in stages I and II) vs those with CKD IV (39%). Although half of the patients are nephroprotected by RAASI, 29% of them have a dose lower than the average dose.

Srita Gabriela Melchior - Secretaria de la Unidad.

Hyperkalemia in kidney transplant recipients according to CKD Stage (K DIGO Guidelines)

<table>
<thead>
<tr>
<th>Stage</th>
<th>n</th>
<th>I-II</th>
<th>IIIa</th>
<th>IIIb</th>
<th>IV</th>
<th>V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperkalemia (n%)</td>
<td>149</td>
<td>115</td>
<td>109</td>
<td>61</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>ACEi – ARB treatment (n%)</td>
<td>60 (44.3%)</td>
<td>48 (45.22%)</td>
<td>56 (61.47%)</td>
<td>37 (72.13%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

P8.063

Single-Cell Analysis Reveals Immune Landscape in Kidney Transplant Recipients With Antibody-Mediated Rejection

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Introduction: Antibody-mediated rejection (ABMR) is the leading cause of future graft loss. A comprehensive understanding of the immune landscape in ABMR is still lacking. Here, we aimed to define the transcriptional landscape of ABMR at single-cell resolution by using single-cell RNA sequencing (scRNA-seq).

Method: Single-cell transcriptomes from one acute antibody-mediated rejection (AMR) biopsy sample was generated. Single-cell transcriptomes of a healthy adult kidney and a chronic antibody-mediated rejection (CAMR) biopsy sample were obtained from the public databases. Unsupervised clustering analysis was employed to identify cell types of the biopsy specimens. Gene set enrichment analysis (GSEA) was used to explore functional differences. Intracellular and intercellular communication pathways were performed to find crosstalk between cell subpopulations.

Results: A higher proportion of endothelial cells was found in the CAMR group. The AMR group had a higher proportion of plasma cells and T/NK cells. The overexpressed genes in rejection group were mainly involved in inflammatory signaling pathways and rejection-related pathways. Compared with the control group, M1-like subtype macrophages were increased in the rejection group. Our results also showed that macrophages/dendritic cells and endothelial cells possessed the most interaction pairs with other immune cells, especially in the AMR group.

Conclusion: Our study provides new insights into AMR and offers a reliable reference for studies on ABMR in kidney transplantation.
P8.064

Development and Validation of a Nomogram for Remnant Kidney Function After Living-Donor Donation

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1Department of Kidney Transplantation, The First Affiliated Hospital of Xi’an Jiaotong University, Xi’an, People’s Republic of China.

Introduction: To develop and validate a nomogram to predict remnant kidney function after living-donor kidney donation.

Method: For nomogram construction and validation, all the donors were randomly divided into two cohorts, including training cohorts and validation cohorts. Then we identified independent prognostic factors using univariate analysis and multivariate logistic regression models. A nomogram for predicting 1-year eGFR was constructed based on these identified prognostic factors. The performance of the nomogram was validated both internally in training cohort and externally in validating cohort.

Results: Age and pre-donation eGFR were significantly identified in multivariate analysis. Finally, a nomogram was constructed by incorporating these two independent predictors. The C-indexes for eGFR prediction in the nomogram were 0.761 and 0.782 for the training set and validation set. The calibration plot showed good agreement between the actual observations and the predicted outcomes both in training set and validation set.

Conclusion: This model might be a simple, but useful guide to predict remnant kidney function after donation, which could be an important clinical tool to improve the selection of living donors.

P8.065

COVID-19 and Pediatric Kidney Transplantation: Iberoamerican Multicentric Study

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Introduction: Concern on the effect of COVID-19 in children recipients of kidney transplant (KT) lead to an initial decline in the transplantation activity. Our aim is to present graft and clinical outcomes of a multicenter cohort of pediatric KT performed during COVID-19 pandemic and compare it with an historic control group. Our secondary goal is to report the clinical evolution of children who suffered COVID-19 after transplantation.

Methods: A retrospective analysis in seven pediatric KT centers of Iberoamerica, from January 2019 to December 2020 was done. In the included institutions, 168 pediatric KT were performed: 97 patients were control group (year 2019) and 71 the study group (year 2020). Baseline demographics and comorbidities were comparable. Graft outcome showed no significant differences in terms of the need of post transplant renal replacement therapy and glomerular filtration rate in the last visit. Graft hydronephrosis, urinary tract infection, and other complications were similar (Table 1).

Results: Six (8.4%) out of 71 patients transplanted in 2020 developed COVID 19 after the transplant. The infection occurred at a mean 71,8 days after the transplant (range: 5-214 days). Three patients were asymptomatic, two presented with fever and one with cough. Three patients were managed on an outpatient basis, two were admitted but remain in a common room, whereas one child required hospitalization in intensive care unit but, without the need of mechanical ventilatory assistance. In 3 patients mycophenolate was suspended, and in the other 3 there were no changes in the immunosuppressive scheme. There were no major respiratory complications such as COVID-19 pneumonia or acute respiratory distress syndrome. Hospital stay was a mean of 13 days (range: 0-39). All six patients had good graft outcome, with no need renal replacement therapy, with a mean glomerular filtration rate of 86,36 mL/min/1.73 m² (range:58 -126). One patient had recurrence of original renal disease.

Conclusion: Despite initial concerns about the increased risk of severe complications of COVID-19 and the graft survival in children with KT, our multicentric series showed similar initial graft outcome and no major respiratory complications. Longer follow up is needed to assess the long-term evolution of these grafts and patients.
Effect of Renal Pre-transplant Desensitization on Renal Graft Function and Survival at 1 and 3 Years

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Background: Kidney transplant is the treatment of choice, offering better quality of life and survival to patients with Chronic Kidney Disease. The use of Immunoglobulin, rituximab and plasma exchange in sensitized patients as desensitization therapy, allows Renal Transplantation by shortening waiting list times, acceptable results, improvement in quality of life and long-term survival of the patient compared to those who remain in dialysis. However, most of the published studies on desensitization approaches have limitations and therefore need to be analyzed further. The objective of the study was to describe the effect of desensitization prior to kidney transplantation on renal graft function and survival at 1 and 3 years.

Methodology: Observational, retrospective, and analytical study nested in a retrospective cohort of adults treated at the Hospital General de Mexico during the period from 2011 to 2020, with living donor kidney transplantation, undergoing and not undergoing desensitization therapy according to institutional protocol. Statistical analysis: descriptive statistics, comparison of variables between groups applying the Mann Whitney U test and Fisher’s exact test. Survival using Kaplan Meyer curves and the difference between populations using the log rank test (p < 0.05, 95% CI).

Results: 28 patients in total, 50% patients did not receive desensitization therapy and 50% received desensitization therapy. 67.8% were men. The average age was 33 years. 17.8% of patients developed antibody-mediated rejection, of which desensitized patients were 21.4% and non-desensitized patients were 14.2%. When comparing groups, no statistical significance was found (P=0.581).

Conclusions: Desensitization therapy in patients with high immunological risk is an option to consider in those patients highly sensitized to a living donor.

<table>
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<tr>
<th>VARIABLES</th>
<th>TOTAL n = 28 (100%)</th>
<th>Desensitized n = 14 (50%)</th>
<th>Not Desensitized n = 14 (50%)</th>
<th>P</th>
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</thead>
<tbody>
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<td>32 ± 10</td>
<td>35 ± 12</td>
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<tr>
<td>Gender</td>
<td>Male</td>
<td>19 (67.8)</td>
<td>8 (42)</td>
<td>11 (57.9)</td>
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<tr>
<td>HAS</td>
<td>Si</td>
<td>22 (78.5)</td>
<td>11 (50)</td>
<td>11 (50)</td>
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<td>DM</td>
<td>Si</td>
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<td>12 (85.7)</td>
<td>11 (78.5)</td>
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<td>B</td>
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<td>Blood transfusion</td>
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<td>Warm ischemia time*</td>
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<td>6 ± 1</td>
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<td>97.6 ± 36.6</td>
<td>96 ± 35</td>
<td>100 ± 40</td>
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<td>26 (92.8)</td>
<td>12 (46%)</td>
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<td>28 (100)</td>
<td>14 (100)</td>
<td>14 (100)</td>
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*minutes

Table 1. Demographic characteristics of the population
P8.067
Catastrophic EBV Infection After Cadaveric Kidney Transplantation

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Introduction: We presented a catastrophic EBV infection after cadaveric kidney transplantation in this study.

Method: Case: 42 years male patient, (unknown primary kidney disease, uneventful hemodialysis duration was 9 months) was transplanted kidney from cadaveric donors. The donor was 30 year old man with a history of Chron’s disease and multiple colonic surgery. ATG was used 5 days as a induction agent. Graft functioned immediately and well. Takrolimus, MMF and prednisolon were used for maintenance immunosuppression. Early posttransplant period was uneventful. The patient was discharged with good clinical condition and his creatinin level 1.9 mg/dl in posttransplant 7th day.

Results: He was admitted to hospital with dry cough and fever in the first month. Leukopenia was remarkable 2000/mm3. Meropenem and G-CSF were started with the diagnosis of febrile neutropenia. Blood and urine culture and CMV-DNA were negative. Splenomegaly was remarkable in his physical examination. EBV-DNA was determined as a 314 000 copy/ml. While the preoperative EBV-IgG of the recipient was positive, there was no information about the donor. Thoracic and abdominal CT’s did not support the diagnosis of PTLD. PET-CT was normal because of persistant fever. The diagnosis of hemophagocytic lymphohistiocytosis associated with EBV reactivation by bone marrow biopsy was made. In addition, EBV-associated acute tubulointerstitial nephritis was detected in allograft biopsy. Aggressive treatment was initiated because of active EBV infection and related hemophagocytic lymphohistiocytic syndrome. While reducing immunosuppressive therapy, high dose dexametazone, etoposide and rituximab were administered according to HLH94 study. The EBV-DNA count, which rose to 768 000, dropped to 28 000, but after about 1.5 months, her breathing was disrupted and taken to intensive care. CMV infection was added to the clinical picture. Ganciclovir started. The patient did not respond to all treatment approaches and posttransplant died on day 96. Later, it was learned that the other recipient who had undergone kidney transplantation in other centers from the same cadaver died at 1 month and the liver recipient died at posttransplant 3rd day. EBV-DNA titers were high in both patients.

Conclusions: As a result, EBV serology should be requested especially from cadaveric donor candidates who have received immunosuppressive treatment and have excessive comorbidity and donors with active infection should be excluded.

We presented a catastrophic EBV infection after cadaveric kidney transplantation in this study.

P8.068
Post-transplant Recurrence of Masked Monoclonal Gammopathy of Renal Significance in a Patient With C3 Glomerulonephritis: A Case Report

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Introduction: Monoclonal gammapathy of renal significance (MGRS) is a recently defined group of renal diseases caused by monoclonal immunoglobulin secreted by nonmalignant proliferative B cell or plasma cell causes renal damage. Here we report a case known as primary kidney disease C3 glomerulonephritis but after kidney transplant diagnosed MGRS.

Case presentation: A 32-year old man underwent live related renal transplant in December 2020 for ESRF secondary C3 glomerulonephritis. At 2 months post-transplant, his serum creatinin levels increased from a baseline creatinine of 1.2 mg/dl to 1.7mg/dl, and he developed proteinuria (1.2 gr/day). Renal biopsy showed monoclonal membranoproliferative glomerulonephritis. His serum and urine kappa/lambda light chain ratio was normal and he had no monoclonal protein in serum and urine immunfixation electrophoresis. After the patient was treated with Rituximab (4 cycles), his serum creatinin levels and proteinuria increased and repeat biopsy showed increase of monoclonal immun complexes in glomerular capillars. The patient was treated bortezomib-based chemotherapy (4 cycles). Repeat biopsy showed no regression renal pathology. His renal functions and proteinuria continued to deteriorate. There were a rise in urine kappa/lambda light chain ratio. He received no further chemotherapy, a decision was taken to manage her kidney condition conservatively.

Conclusions: Monoclonal immunoglobulin deposits may not be detectable in standard immunofluorescence techniques and can result missing the diagnosis of MGRS. Patients with C3 glomerulonephritis should be examined in detail for monoclonal gammapathy before kidney transplantation.

Case report.
A Case Report: HLA Antibodies in Temporal Relation To Vaccination in an End-Stage Renal Disease Pediatric Patient on the Renal Transplant Waiting List

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Introduction: Due to an increased risk of infection after transplantation vaccinations should be administered before the procedure whenever feasible. The association between infection and autoimmunity among genetically predisposed individuals has been demonstrated. Some cases of de novo occurrence of HLA antibodies following vaccination against influenza, pneumococcus, hepatitis B, and COVID-19 have been documented. Many plausible pathways for the production of HLA antibodies (Abs) induced by vaccination have been proposed, such as encouraging T and B cells to respond to vaccination antigens that cross-react with HLA proteins, the release of cytokines that reactivate memory response, and the effect of vaccine adjuvants. We present the case of a girl with ESRD with transient HLA antibodies in temporal relation to vaccination.

Case: 5-year-old female, diagnosed with autosomal recessive polycystic kidney disease, ESRD, mild liver fibrosis. No genetic study is available. Premature birth due to severe oligohydramnios, with creatinine 0.8mg/dL, metabolic acidosis, and arterial hypertension. She is in conservative treatment for ESRD until age 4 when she enters the continuous outpatient peritoneal dialysis program. No history of blood transfusions. In 2021, she receives the following vaccines, March: anti-influenza (annual dose), May: varicella vaccine (booster), May, June, and September: Hepatitis B vaccine (double dose) without seroconversion, thus the scheme was repeated in October and November. In October 2021, histocompatibility studies were carried out: HLA Typing (ISSO-Luminex) A*02:30; B*44:51; DRB1*04:07; HLA Ab screening with single Antigen Bead (SAB), Class I: B76 (MFI 1500-3000); Class II: DR4, DR7, DR9 (MFI 3001-5000). Note that anti-DR4 and DR7 antibodies appear to be autoantibodies (although there is no high-resolution typing available to confirm that the Abs are specific to self HLA antigens). The SAB was repeated after one month, using a different brand of reagents, obtaining identical results. After four months, in February 2022, a third serum sample was tested with SAB, this time with a negative result for HLA Abs.

Conclusion: Current clinical guidelines recommend vaccination of solid organ transplant candidates against various pathogens. The development of de novo antibodies against HLA after an external stimulus different from HLA antigens is possible. More studies are needed to better understand this post-vaccination phenomenon and its clinical implications.
Sex Differences in Acute Kidney Injury Following BD - An Isolated Rat Organ Perfusion Model

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Introduction: Clinical studies associated female donors’ kidneys with poor outcomes in male recipients. Brain death (BD) leads to hemodynamic and immunologic alterations impacting organ viability. Following BD, female rats present higher renal inflammation correlated to female sex hormones reduction. Here, we aimed to investigate differences between sexes in the renal injury and function triggered by BD using an isolated rat kidney perfusion (IPK) model.

Methods: Female and male Wistar Rats (8 weeks) were preserved following BD for 4h. Sham-operated (S) rats were performed as controls. Left kidneys were collected and maintained in a cold saline solution (30 min). Normothermic IPK (90 min) was performed with Williams Medium E (WME) perfusion fluid. Renal injury and function were estimated by renal morphology analyses, staining of complement system components and inflammatory cell markers, monitoring creatinine clearance, and renal perfusate flow.

Results: BD-female kidneys presented higher eNOS expression (P=0.0048). Regarding renal flow, BD-males kidneys presented a reduced flow in the IPK (P<0.0001). After IPK, both sexes presented increase in complement system formation/deposition (C5b-9: Pglom=0.0166, Pint<0.0001; C3d: Pglom=0.0008, Pint=0.0105), myeloperoxidase (Pglom=0.0043, Pint<0.0001) and perfusate IL-6 (P=0.0126). Analysis of relative gene expression in perfused kidneys from BD rats revealed a similar upregulation of inflammatory profile in both sexes (IL-1β, IL-6, and eNOS -P<0.0001), how ever P-selectin (P=0.0001), iNOS (P=0.0002), Caspase-3 (P<0.0001) and BCL-2 (P=0.0153) increased in BD-female kidneys and KIM-1 (P=0.0191) in BD-male kidneys.

Conclusions: Our data showed that despite the inflammatory response similarly found in both sexes, BD leads to renal hyperperfusion in males. The maintenance of perfusion in females seems to be correlated with greater endothelial nitric oxide synthase (eNOS) expression due to high estradiol concentration prior to BD. Once normothermic IPK allows graft assessment and therapeutic drug delivery under physiologic conditions, such findings support further studies emphasizing vascular preservation and anti-inflammatory therapies to order to improve renal graft quality.

Changes in the Kidney Allocation Model in Uruguay - HLA Compatibility vs. Time on Waiting List

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Introduction: The Instituto Nacional de Donación y Trasplante (INDT) implemented two years ago the new kidney allocation model (new model -NM), previously evaluated with mathematical model that allowed to simulate scenarios and evaluate the impact on allocations. The NM maintains a mixed flow and scoring system as the Previous model (PM), but establishes changes in ABO compatibility and the weighing of: time wait list (TWL), HLA compatibility and donor (D) and recipient (R) age (Table 1). The aim of this work is to characterize and compare the groups of patients assigned under both models (NM and PM), in relation to: recipient age, TWL, ABO compatibility and HLA compatibility score.

Methods: The population studied included the recipients assigned during 1/2018-02/2020 (PM) and during 03/2020-03/2022 (NM) which were obtained from the database of the INDT’s Assignment Unit (Table). We reviewed the following variables of 1st and 2nd recipients assigned: D and R ABO, R age, TWL, and HLA compatibility recorded as numerical value. Variables categorized were: age (0-18/19-60/over 61 years), ABO compatibility with donor (isogroup/compatible). Statistical analysis was applied.

Results: Total allocation records analysed were N=405, 205 corresponding to PM and 200 to NM. With the new model, 25(12%) compatible ABO recipients were assigned, while in PM all allocations were ABO isogroup. NM allocated patients with higher WLT than PM (U13887, p<0.05- Mann Whitney U test). NM allocated patients with lower HLA compatibility score than PM (D=0.3145, p<0.05, Kolmogorov-Graph). Age range comparison did not show differences (p > 0.05 Chi-square 11.8176).

Conclusions: The comparative analysis of both models shows differences in HLA compatibility and TWL in recipients assigned. The decrease on HLA compatibility score is explained in the first two years of NM implementation by the allocation on patients with long TWL.

<table>
<thead>
<tr>
<th>Allocation variables</th>
<th>Previous Model PM</th>
<th>New Model NM</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEDIATRIC</td>
<td>&lt; 15 years</td>
<td>&lt; 18 years</td>
</tr>
<tr>
<td>WEIGHTING OF TIME ON THE WAITING LIST</td>
<td>5 years 0.5 points 6 years 0.7 points 7 years 0.9 points 8 years 1.1 points 9 years 1.3 points 10 years 1.5 points</td>
<td>Reaching:*</td>
</tr>
<tr>
<td></td>
<td>- Average time: 1.33 points</td>
<td>- Maximum time: 8 points</td>
</tr>
<tr>
<td>WEIGHTING OF HLA COMPATIBILITY</td>
<td>Up to 8 points depending on compatibilities</td>
<td>*relative to the entire list</td>
</tr>
<tr>
<td>BLOOD GROUP ABO</td>
<td>Same group</td>
<td>Compatible: Donor O - Recipient O and B Donor A – Recipient A and AB</td>
</tr>
</tbody>
</table>

Graph: HLA compatibility score comparative
Serial Plasma Exchange Is a Promising Effective Method in Blood Hemagglutinin Level Reduction

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Introduction: Severe donor shortage in kidney transplantation stimulates trails of live-related transplants across the ABO antibody barrier. Successful desensitization was achieved by repeated plasmapheresis (PP), splenectomy, donor thrombocyte transfusion, together with intensified immunosuppression. This study estimates the effect of serial sessions of plasma exchange on the blood group’s antibody titer.

Method: This is a pilot study that included 25 patients on plasma exchange for different causes with albumin replacement. Excluding patients using plasma replacement during sessions, positive direct and indirect antiglobulin test, and AB blood group. Blood group antibody titer was measured by gel card titration method before starting plasma exchange and after each session for five sessions.

Results: This study showed that blood groups (A), (B), (O) was 12, 8, 5 patients respectively. The Baseline Anti (A) and Anti (B) antibodies titer before plasma exchange were (median [IQR] 128, 600 [64–256] and 64 [64–128]) respectively with significant reduction after 5 sessions with (median [IQR] 1 [0–4] and 2 [1–2]) respectively p value <0.001, 0.001 respectively. Anti (A) and Anti (B) antibodies titer reduction percent after 1st session (mean±SD -47.06±12.3% and -50.00±17.68%) respectively reaching after 5th session (mean±SD -97.93±0.99% and -99.04±0.72%) respectively. Anti (A) and Anti (B) antibodies titer were negatively correlated with patient’s age (r -0.793 P <0.001, r-0.731, p 0.005) respectively. Patients with age <50 (N=13) years has higher baseline Anti (A) and Anti (B) antibodies (median [IQR] 256 [256–512], 128 [128–128]) respectively compared with patients with age >50years (N=12) (median [IQR] 64 [64–64], 64 [48–64]) respectively p value 0.002, 0.001 respectively. Also on comparing Patients on immunosuppressive drugs (N= 14) and without immunosuppressive drugs (N=11) there was no significant difference in baseline Anti (B) titer (median [IQR] 64[64–128] vs 96[64–128]) p value 0.53 while baseline Anti (A) titer was significantly higher in patients without immunosuppressive versus patients with immunosuppressive drugs (median [IQR] 256[256–512] vs 64[64–96]) p value 0.01 and the titer after 5th session (median [IQR] 4 [4–4] vs 0.5[0–1]) p-value 0.01.

Conclusion: Serial plasma exchange is an effective method for blood hemagglutinin reduction. Antibody titer was affected by age of patients and immunosuppressive drugs had a significant effect on Anti (A) antibody titer.
**P8.079**

Systematic Review and Meta-Analysis on the Effect of Blood Transfusions on Kidney Transplant Outcomes: Shining New Light on an Age-Old Debate

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**Introduction:** Since the 1970’s, the use of transfusions in kidney transplant medicine has been a point of contention. While they are a solution to the anaemia plaguing this patient population and in 1978 were shown to lead to a dose-dependent improvement in graft survival, they also have the ability to induce a sensitized state, increasing the risk for poorer graft outcomes. Influenced by the inherent risk, clinicians have begun to administer transfusions based on clinical need as opposed to deliberately. Furthermore, the popularity and efficacy of tacrolimus as an immunosuppressant over the past two decades, has allowed for a degree of standardization across different kidney transplant centres. The majority of the studies in the past two decades have focused on previously understudied postoperative blood transfusions, occurring in 40-60% of cases. No systematic reviews or meta-analyses have been published including these newer studies. With these details in mind we believed it prudent to undertake a systematic review and meta-analysis exploring the effect transfusions have on transplant outcomes.

**Methods:** A systematic search was conducted using MEDLINE, Embase, Cochrane library and Clinicaltrials.gov. Including only English articles published between 1/1/2000 and 01/03/2022, we found 9 studies that met our inclusion criteria. A meta-analysis was thereby carried out for three outcomes, delayed graft function (DGF), the development of de novo donor specific antibodies, and antibody mediated rejection (AMR).

**Results:** Low-level evidence exists for no difference or an increase in DGF and AMR for participants who received at least one blood transfusion. Low-level evidence exists for an increase in AMR for participants who received at least one blood transfusion. For the outcomes not included in the meta-analysis (graft loss/failure, graft survival, acute rejection, development of HLA-Abs, sepsis), each of the included studies reported either no difference or a detrimental effect on the outcomes. No study reported any improvement with blood transfusion usage.

**Conclusion:** The transfusion effect appears not to exist in the 21st century even in patients receiving postoperative blood transfusions. However, while transfusions are avoided wherever possible and despite a myriad of replacements becoming available, transfusions in kidney transplant recipients do not appear to be associated with any worse outcomes compared to their non transfused counterparts. While more research is required, clinicians may be able to administer blood transfusions to kidney transplant patients with a clear conscience.

**P8.080**

Prevalence of New Onset Diabetes After Transplantation in Native Africans

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**Introduction:** Very little is known about the prevalence of New onset diabetes after Transplant (NODAT) in Sub-saharans and Eastern Africans. Most of the data are related to African Americans and North and South Africa. The aims of this study were to examine the prevalence of NODAT in Sudanese renal transplant population and to compare it with the published literature and to identify the risk factors for developing NODAT.

**Materials and Methods:** 150 patients who underwent live-related kidney transplant during the period January 2015 to January 2016 were included in this study. Diabetic patients were excluded. Follow-up was for 2 years post-transplant. The variables studied were age, sex, body mass index, calcineurin inhibitor used, family history of diabetes mellitus (DM), pre-transplant steroid therapy, dyslipidemia and hepatitis C virus infection.

**Results:** Twenty three patients (15.3%) developed NODAT during the study period. On multivariate analysis, the risk factors for developing NODAT were: A family history of DM (p=0.01), and pre-transplant steroid therapy (p=0.01).

**Conclusion:** The prevalence of NODAT in this study population was significantly lower than the reported prevalence in African Americans. The newly reported finding of the association between pre-transplant steroid therapy and NODAT warrants further investigation.
Differential Control of Systolic and Diastolic Blood Pressure in Renal Transplant Recipients

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Background: Differential control of systolic and diastolic blood pressure is well documented in the treatment of hypertension in general population1-2 but there is limited data in renal transplant recipients.

Method: A single-center retrospective study of the renal transplant recipients who underwent kidney transplantation between January 2017 to May 2020 with12 months follow up. We reviewed BP readings before transplant and at one month, six months, 12 months after kidney transplantation. We also reviewed the number of BP medications at the same intervals post transplantation. BP goal was <140/90. during the time of this retrospective study as per the published guidelines3.

Results: Conclusion: Diastolic blood pressure seemed much easier to control than systolic BP in the first year and it required significantly less number of medications to control. A metaanalysis will be helpful to confirm this interesting observation.

References:
Weight Gain in the First Year Post Renal Transplantation

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Background: Undesirable weight gain following renal transplantation is relatively common. This study examined the incidence and risk factors for weight gain of >5% in the first post-transplantation year at our center.

Method: A single-center retrospective study of the renal transplant recipients who underwent kidney transplantation between January 2017 to May 2020 with 12 months of follow-up. We reviewed the patients’ demographics, weight changes, and A1C values. We also examined the factors associated with weight gain >5%.

Results: 287 renal transplant recipients were included. 74% were ≥ 30 years, 58% were men and 80% were living-donor kidney recipients. Preemptive transplantation was 10.1%, PD: 11.5% and HD: 78.4%. At baseline, obesity stage 1 (BMI: 30-34.9) was present in 20.2% of patients and obesity stage 2 (BMI 35-39.9) was present in 4.2%. Diabetes (DM) was present in 99 (34.5%), [DM type I: 25 (25.3%) and DM type II: 74 (74.7%)]. The average weight gain by one year of the transplant was 6.0±8.3 (Kg), and 59.6% of patients had a weight increase of ≥5%. Both males and females significantly gained weight to a comparable degree (P: 0.588). Weight gain after a living donor kidney transplant was much more than after a deceased donor kidney transplant [6.63 Kg (5.58 to 7.69) versus 3.42 Kg (1.12 to 5.71), P: 0.009]. Multivariate analysis showed that the odds ratio of weight gain ≥ 5% after a living donor (versus deceased donor) kidney transplant was OR: 2.86 (CI: 1.49 to 5.523, P: 0.002). Baseline BMI was negatively associated with weight gain post-renal transplantation (OR:0.9, CI: 0.854 to 0.949, P: <0.00). Age, gender, DM, and HTN were not associated with higher weight gain.

Conclusion: About two-thirds of the renal transplant recipients gained at least ≥5% of their baseline weight by the first year after kidney transplantation. Recipients of living donor kidney transplants and those with lower BMI were at increased risk.
Renal Transplantation and Statins Effects on Dyslipidemia in Renal Transplant Recipients

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Purpose: To review the effect of renal transplantation and adding of statins on dyslipidemia in renal transplant recipients.

Methods: A single center experience retrospective study of renal transplant recipients, from 2017 to 2020. Lipids' profile and Hgb A1C were reviewed at baseline (before transplant) and at average 12 months follow-up of renal transplant recipients who received statins or not.

Results: 287 renal transplant recipients were included. 74% were ≥ 30 years, men: 58% and living-donor kidney recipients: 80%. Statins were prescribed to 80% of kidney recipients who were ≥30 years old and to 33% who were <30 years old. 28% of the recipients were already on statins before the renal transplantation. Whereas statins were initiated in 26% before discharge from the transplant admission, or during the first year in 14%. While 32% did not receive any statins. The most common statin used was Atorvastatin at 10mg in 60% or 20mg in 23% of the cases. In patients who did not receive statins: renal transplantation was associated with a significant increase of total cholesterol (TC) by 0.31 mmol/L (0.04 to 0.59; P: 0.026) and a significant increase of LDL by 0.40 mmol/L (0.16 to 0.65; P: 0.001). On the other hand, and despite weight gain of average 6.9 kg (P <0.001), and increased A1C by 0.71 (P<0.001); renal transplantation was associated with an increase of HDL by 0.17 mmol/L (0.09 to 0.25; P<0.001) and down trending but not statically significant decrease of triglyceride (TG) by -0.09 mmol/L (-0.25 to 0.07; P: 0.280). In renal transplant recipients who received statins: despite weight gain of 5.6 kg (P<0.001) and increased A1C by 0.93 (P: <0.001), HDL improved by 0.17 mmol/L (0.13 to 0.22; P<0.001) and TG decreased by -0.34 mmol/L (-0.50 to -0.17; P<0.001). Statins were associated with a numerical decrease of TC by -0.06 mmol/L (-0.23 to 0.12; P: 0.519) and nonsignificant increase of LDL by only 0.04 (-0.10 to 0.18; P: 0.607). Statins were significantly associated with improvement of TC and LDL compared to no statins. The mean changes of TC (from baseline to 12 months) while on statins versus none were (-0.06 mmol/L ±1.16 versus 0.31 mmol/L ±1.12; P: 0.026) and the mean changes of LDL while on statins versus none were (0.04 mmol/L ±0.96 versus 0.40 mmol/L ±1.02; P: 0.008).

Conclusions: Despite weight gain and the increased level of A1C seen after renal transplantation, renal transplantation was associated with improved TG and HDL. Adding statins in patients at higher risk of dyslipidemia not only maintained the beneficial effects of renal transplantation on HDL and TG but also had significant “buffering” effect against the rising of TC and LDL.
Outcomes of Post Kidney Transplant Lymphoproliferative Disorder (PTLD)

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Introduction: Common malignancies post kidney transplantation are non-melanotic skin cancer, Kaposi sarcoma and post-transplant lymphoproliferative disorder (PTLD). We aim to study the outcomes of PTLD in KT recipient in oncology center in UAE.

Method: Ethical approval was obtained to conduct a retrospective chart review study at Tawam Hospital (January 2009 to 2021). We included adult kidney transplant recipients (age > 16) diagnosed with PTLD. Demographic, laboratory data and clinical outcomes were studied.

Result: 528 KT recipients were identified during the study period, and 6 patients (1.13%) were included. The mean age was 47.5 years, four females and two males. All the KT patients received transplantation from living donors and were on maintenance triple immunosuppressive (IS) medications prior to PTLD diagnosis. The comorbid conditions in our cohort were hypertension (100%), diabetes mellitus (50%), ischemic heart disease (33%), history of rejection (33%), hepatitis B virus (33%) and hemolytic uremic syndrome (16.6%). The types of PTLD (n=6) in our cohort were Diffuse large B-cell lymphoma (n=4), Anaplastic Large Cell Lymphoma of left breast (1), and H. pylori related gastric maltoma (n=1). The median diagnosis interval ranged between 3 to 27 years post transplantation. The medical management included reduction of IS medications in all patients (n=6), Four PTLD patients required chemotherapy R-CHOP and patient with gastric lymphoma was treated with H pylori eradication. One patient developed recurrence of lymphoma DLBCL at 30 years post kidney transplantation and was offered palliative care due to old age and sarcoidosis conditions. Mortality rate was 33% (n=2) related to septic shock with gram-negative bacteremia.

Conclusion: The incidence of PTLD in our KT recipients over 10 years was 1.13 %. Late onset PTLD at 3 to 27 years were noted in our cohort, and recurrent disease is very rare.

Persistent Hyperparathyroidism Post Renal Transplantation

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Background and Aim: Hyperparathyroidism (HPT) is a frequent complication in chronic kidney disease and may persist in 20 to 50% of cases one year after kidney transplantation; and may contribute to long term allograft dysfunction and increased risk of fractures. There is scant data on the prevalence of post-transplant HPT in kidney transplant patients in Saudi Arabia. The aim of this study is to evaluate the prevalence of this complication and to identify its risk factors in a single center in Saudi Arabia.

Methods: In a retrospective study, data of 287 kidney transplant recipients, who underwent kidney transplant between January 2017 and May 2020, have been collected which included demographic characteristic, history of hypertension, diabetes mellitus, coronary artery disease, duration of dialysis therapy, dialysis modality, and type of vascular access. Serum iPTH measured prior to transplant then every 6 months post-transplant for 2 years.

Results: Of 287 kidney transplant recipients: 119 (41.5%) were diabetic and 38 (13.2%) had coronary artery disease. 231 (80.5%) had received living-donor kidneys and 56 (19.5%) were cadaveric recipients. iPTH was before transplant: 82.2±84.2, 1- 6 months: 27.5±31.4, 6-12 months: 28.8±35.9, and 12-24 months: 30.1±43.3. P value <0.001. Persistent hyperparathyroidism was found in 47 (16%) of patients at one year post renal transplant. The presence of diabetes mellitus as well as the duration of dialysis were predictors of persistent HPT. Type of transplant and allograft function did not seem to have any correlation.

Conclusion: In a single center experience, (16%) of kidney transplant patients had persistent HPT and the presence of diabetes mellitus and the duration of dialysis were important risk factors in its development.
Semaglutide May Be Safe After Kidney Transplant

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Background: The most common cause of end-stage renal disease (ESRD) is diabetes mellitus (DM). Kidney transplantation offers better outcomes for ESRD patients. Patients could develop post-transplant DM (PTDM). Management of DM after transplantation (whether the patient had it from before or after the transplant) is challenging. Different medications could be used to manage PTDM. Those medications have good safety and efficacy record in general population and patients with mild degrees of kidney disease. At the same time, weight gain is a major issue after kidney transplant.

Methods: We conducted a retrospective single center analysis of safety and efficacy of Semaglutide after kidney transplantation. The study was approved by institutional review board. We collected data (demographics, laboratory tests and any symptoms or hospitalizations) for 28 patients for 12 months.

Results: All 28 patients took subcutaneous Semaglutide at an average of 0.5 mg/week throughout the study period. Patients’ average age was 64. Thirteen were females and all from Middle Eastern decent and had kidney transplant on average of 29 months when they were included in the study. Eleven patients had DM before the transplant and the rest had PTDM. 15 patients were on metformin and 10 were on insulin while the rest were not on any other medications at the start of the study. Baseline average creatinine was 1.2 mg/dL (106.3 mmol/L) and glycated hemoglobin (HbA1c) of 8.4 g/dL at the start of the study while creatinine was 1.1 mg/dL (97.5 mmol/L) and HbA1c was 7.1 g/dL at the end. HbA1c dropped 1.2 on average within 6 weeks of starting Semaglutide and stayed around the same level for the rest of the study. Urine protein decreased significantly within 6 months and was maintained throughout the study. One patient developed unstable angina during the study and another one was hospitalized with acute pancreatitis. A third patient developed bacterial pneumonia. Ten patients had nausea and vomiting after starting Semaglutide but that resolved 2 weeks later with lowering the dose. No allergic reactions or hypoglycemia episodes were recorded. The average weight dropped 3.1 kg throughout the study and body mass index changed from 28.9 to 27.3. Only one patient stopped the medication during the study (the one who had acute pancreatitis).

Conclusion: In this retrospective analysis, Semaglutide seems to be safe and efficacious after kidney transplantation. It can be considered to manage DM after transplantation.
Heart-Kidney Team: Cardiovascular Profile and Outcomes in Kidney Transplant Candidates

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1Cardiology Department, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 2Nefrology Department, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Introduction: Renal transplant is one of the most important treatments in the end stage of chronic kidney disease (CKD). This treatment improves quality of life and reduces mortality compared to patients who remain on dialysis. However, it is known that kidney transplant candidates have multiple comorbidities, which must be carefully evaluated, because they have an important influence on the perioperative risk and post-transplant survival. In addition, cardiovascular disease is the mean cause of death in patients with CKD and in kidney recipients. Therefore, an adequate heart-kidney team evaluation prior to transplantation is essential, not only to prevent perioperative complications, but also to improve short- and long-term results in the post-transplant stage. The opportunity to detect the presence of coronary disease in asymptomatic patients makes possible the implementation of therapeutic strategies prior to kidney transplant and provides useful information to reduce perioperative cardiovascular risk and mortality in these patients. Despite this, the presence of cardiovascular disease could determine the transplant contraindication in certain situations. Up to the present, there are no single consensus on cardiac evaluation in kidney transplant candidates, and the methods chosen for screening for cardiovascular disease are still empirical. The objectives of the study are to determine: (1) history of major adverse cardiac events at the time of the kidney transplant evaluation, (2) proportion of patients in whom stress tests and/or coronary angiography were requested (3) patients underwent coronary revascularization (4) incidence of major cardiac adverse events in kidney transplant recipients and (5) incidence of cardiovascular mortality in the follow-up.

Method: A cross-sectional study from January 2010 to December 2019 was performed from a university hospital in Buenos Aires, Argentina. Kidney transplant candidates >18 years with previous hear-kidney team evaluation were included.

Results: A total of 153 patients [median age 42.7 years (SD 14.4), 60.8% men] were included in the study. Globally, the prevalence of type 2 diabetes mellitus in the population was 5.2% and 67.5% of patients were hypertensive. Importantly, 22.2% and 89.5% showed a history of cardiovascular disease and prior renal replacement therapy, respectively. In addition, 18.3% and 2.6% of the population required a stress test and coronary angiography, respectively. Baseline characteristics are shown in Table 1. Finally, 1.96% presented cardiovascular events and one patient had cardiovascular death during one year of follow-up.

Conclusion: Despite an exhaustive evaluation in kidney transplant candidates, cardiovascular events after renal transplant at one year continue to be significant. This highlights the complexity of the population evaluated and the need to continue improving the heart-kidney team.

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<th>Table 1</th>
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<td><strong>Variables</strong></td>
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<td><strong>Categorical variables, n (%)</strong></td>
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<td>Male</td>
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<td>Hypertension</td>
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<td>Dyslipidemia</td>
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<td>Coronary artery disease</td>
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<td>Acute myocardial infarction</td>
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<td>Chronic angina</td>
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<td>Coronary angioplasty</td>
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<td>Myocardial revascularization surgery</td>
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<td>Hemodialysis</td>
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<td>Peritoneal dialysis</td>
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**Therapy**

- ACEI: 39 (26.2%)
- ARB: 25 (16.6%)
- Beta blockers: 51 (34.0%)
- Aspirin: 24 (15.9%)
- Statins: 22 (14.5%)

**Pre Transplantation test**

- Sinus EKG: 153 (100.0%)
- Echocardiogram trasthoracic: 146 (95.4%)
- Stress test: 28 (18.3%)
- Coronary angiography: 4 (2.6%)

ACEI: angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor antagonists, EKG: electrocardiogram
P6.090

Findings of Cardiovascular Workup of Renal Transplant Candidates

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Background: There is limited data about the prevalence of cardiovascular risk factors and the findings of cardiovascular workup of renal transplant candidates. The cardiovascular risk assessment of renal transplant candidates at our center is driven mostly from American Heart Association guidelines 2013. Screening echo is performed to all renal transplant candidates. PET stress nuclear test is done to those who have ≥3 cardiovascular risk factors, limited functional status or abnormal echo findings. Decision of cardiac catheterization is differed to cardiology’s assessment. Abdominal/ pelvis CT scan with intravenous contrast is done to evaluate the extent of pelvic vascular calcifications and atherosclerosis. Patients on peritoneal dialysis (PD), undergoing preemptive transplantation or at low surgical risk are typically excluded. Here we studied the prevalence of cardiovascular risk factors and the findings of cardiovascular workup of renal transplant candidates at our center.

Method: A single-center experience retrospective study of renal transplant candidates who underwent renal transplant from January 2017 to May 2020. We reviewed their cardiovascular risk factors and the results of their pretransplant cardiovascular workup.

Results: 287 renal transplant recipients were included. 74% were ≥ 30 years, 58% were men and 80% were living-donor kidney recipients (LKT). Preemptive transplantation was 10.1%, PD: 11.5% and HD: 78.4%. At one year, 70.1% of the patients reached the target BP goal. Systolic BP was 124 ± 19.1 at baseline, and it improved by 5.25 (-7.5 to -3) by 12 months. P-value <0.001. These changes were observed in both genders and at a comparable difference (P: 0.579 for SBP, P: 0.136 for DBP). The number of blood pressure medications also significantly decreased.

Conclusion: Our study demonstrated the positive effect of kidney transplantation on systolic and diastolic blood pressure in the first year post-transplantation in both genders. In addition, the number of blood pressure medications also significantly decreased.

Reference:

P6.091

The Impact of Kidney Transplantation on Systolic And Diastolic Blood Pressure and the Number of Blood Pressure Medications in the First-Year Post- Kidney Transplantation

Ziad Arabi1,2,3, Elwaleed Elhassan1,2,3, Mubarak Abdalla1,2,3
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Background/ Aim: To examine the impact of kidney transplantation on systolic and diastolic blood pressure and the number of blood pressure medications in the first year post-kidney transplantation at our center.

Method: A single-center retrospective study of the renal transplant recipients who underwent kidney transplantation between January 2017 to May 2020 with12 months of follow-up. The blood pressure target goal at the time of this retrospective study was <140/90.1 We reviewed BP readings before transplant and at one month, six months, 12 months after kidney transplantation. We also studied the number of BP medications at identical intervals post-transplantation.

Results: A total of 278 renal transplant recipients were included. 74% were ≥ 30 years, 58% were men, and 80% were living-donor kidney recipients. Preemptive transplantation was 10.1%, PD: 11.5% and HD: 78.4%. At one year, 70.1% of the patients reached the target BP goal. Systolic BP was 124 ± 19.1 at baseline, and it improved by 5.25 (-7.5 to -3) by 12 months. P-value <0.001. These changes were observed in both genders and at a comparable difference (P: 0.579 for SBP, P: 0.136 for DBP). The number of blood pressure medications also significantly decreased.

Conclusion: Our study demonstrated the positive effect of kidney transplantation on systolic and diastolic blood pressure in the first year post-transplantation in both genders. In addition, the number of blood pressure medications also significantly decreased.

Number of medications | 1 month | 6 months | 12 months | P (For 1 month vs. 12 months)
--- | --- | --- | --- | ---
0 | 67 (23.3%) | 86 (28.6%) | 84 (29.3%) | 0.001
1 | 91 (31.7%) | 93 (32.4%) | 89 (31%) |
2 | 85 (29.6%) | 83 (28.9%) | 81 (28.2%) |
3 | 27 (9.4%) | 18 (6.3%) | 18 (6.3%) |
4 | 6 (2.1%) | 2 (0.7%) | 6 (2.1%) |
5 | 2 (0.7%) |
Conversion From MPA Twice a Day to MPA Once a Day Following Kidney/ Kidney Transplantation

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Introduction: The incidence of immunological graft loss after the first months of years following kidney transplantation ranges from 30 to 50%. In the majority of cases, non-adherence with the immunosuppressive therapy is considered to be the main reason of rejection. Single daily tacrolimus (Tac) immunosuppression was initiated with the aim of alleviating non-adherence. However, mycophenolate acid (MPA) is almost given in association to Tac but twice a day.

Methods: After a previous pharmacokinetic profile study comparing MPA twice a day versus once a day in 9 kidney transplant patients, we decided in 2017 to prospectively give the total dose of MPA in a single morning oral dose intake to patients already receiving Tac once a day. This was a monocentre observational study. Patients who accepted to participate gave their consent and were switched during a regular out-put clinical visit. We included kidney or pancreas/kidney transplant recipients transplanted at least more than 6 months after surgery. Inclusion lasted 12 months.

Results: Mean follow-up was 16.3 months (6 to 48). 65 patients (53 kidney, 12 pancreas/kidney) were included. 78% (n=51) of recipients received organs from a cadaver donor. 63% (n=41) were not sensitized. Recipient’s mean age was 49.8 years. 40% (n=26) of patients were on steroid maintenance. Mean conversion time to once daily MPA was 33 months after transplantation. Daily dose intake to patients already receiving Tac once a day. This was a monocentre observational study. Patients who accepted to participate gave their consent and were switched during a regular out-put clinical visit. We included kidney or pancreas/kidney transplant recipients transplanted at least more than 6 months after surgery. Inclusion lasted 12 months.

Conclusion: Once daily Tac in association to one daily MPA could represent a good strategy to decrease non-adherence and improve quality of life of transplant recipients.

ABO Incompatible Renal Transplantation in Argentina: Experience in a Tertiary Referral University Hospital

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Introduction: ABO-incompatible renal transplant (ABOiTr) is little used in Argentina despite being able to increase the pool of donors. We report our experience with this modality in the period Jul/2014 – Mar/2022.

Study population and Methods: 177 living transplant donor were performed in the studied period of which 23 were ABOi (13%). Age of Tr:ABOi: 48 years (20-78), 10 female (43%), second Tr 6/23 (26%), time on dialysis 21.8 months (5-60), preemptive 26%, non-related donor 52%, HLA mismatch 3.7 (0-6), presence of DSA in 22%. Median pre-Tr donor anti-group agglutinins: IgG 1/16 (0-1028), IgM 1/8 (0-256). Pre-Tr conditioning therapy included rituximab in 22/23 and plasmapheresis (PF) in 20/23 with a median of 4 sessions (range 1-9). Two patients received PF post ABOi Tr. All received immunosuppression with tacrolimus and mycophenolate one month pre-Tr and continued post-Tr. Intravenous immunoglobulin (IVIG) was used in all patients post last PF and antithymocyte globulin as induction in 20/23 patients.

Results: Mean follow-up post-Tr was 37.4 months (1-92). Six patients developed acute rejection (AMR: 4, TCMR: 2). Rejection treatment included corticosteroids pulses and IVIG in all cases. Bortezomib was used in one case and PF in another. All patients except one responded to treatment. The most frequent post-Tr complications were: urinary tract infections in 7 patients of them with sepsis, BK reactivation in 2 cases and 1 case of immediate post-Tr hemorrhage. Nine patients developed COVID infection (99%), 3 of them required hospitalization. One graft loss was recorded at 6 months post-Tr due to refractory AMR. Three patients died in the study period, two deaths related to COVID infection (1 and 33 months post-Tr) and one death was related to PTLD (49 months post-Tr), all deaths were with a functioning kidney (median patient survival 89%). Creatinine level in last control was 1.53mg/dl (0.90-2.70 mg/dl) and P/C 0.16 (0.1-1.0).

Conclusion: ABOiTr is a feasible alternative in our country, these preliminary results suggest that it should be offered more extensively to recipients who do not have an ABO compatible donor.

Fundación Nefrológica de Córdoba.
Assessment of Urinary Tract Infections Microbiologically in Kidney Transplant Recipients

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Introduction: Urinary tract infection (UTI) is the most common infection after kidney transplantation. Urinary tract infections can be easily treated with antibiotics, but on the other hand, they can have devastating effects up to graft loss. Knowledge of the causative agents and resistance rates annually will be a guide for diagnosis and treatment. In our study, the bacteria isolated from renal transplant recipients that were diagnosed as urinary tract infections are evaluated in kidney transplant recipients for five years.

Method: Since 3 November 1975 we have performed 3304 kidney transplant. We evaluated 546 renal transplant recipients from January 2016 to May 2021 at our transplant center. We evaluated the data of kidney transplant recipients with urinary tract infections. For this purpose medical reports of the patients were reviewed retrospectively. Demographic and laboratory data of the patients recorded retrospectively and analyzed. We defined the most common causative agents, the rate of resistance to widely used antibiotics (ciprofloxasin, trimethoprim/sulfamethoxazole), the rate of extended-spectrum beta-lactamase (ESBL) positivity, extensively drug-resistance (XDR) and pun drug-resistance (PDR).

Results: In the last five years study period, in 146 of 546 renal transplant recipients had identified 363 urine tract infection episodes. This patients were 84 (57.5%) female and 62 (42.46%) male. The median age was 48 (range 18-68). Isolated bacteria were 291 gram negative, 64 gram positive and 16 Candida spp. 135 (37,2%) of the 363 isolates were Escherichia coli, 110 (30,3, ESBL 54%) Klebsiella pneumoniae, 40 (11 %) Enterococcus spp. and 1 (3.2%) between 2016-2021 (Table 1).

Conclusion: Enterobacteriaceae are still the organisms most frequently isolated from UTI in renal transplant recipients. The three most common bacteria were E. coli, K.pneumoniae and Enterococcus spp., similar to previous years. However, ciprofloxacin and trimethoprim/sulfamethoxazole resistance increased during this period. In addition, there was also observed a significant increase in rates of ESBL, XDR and PDR within the years. Infections caused by ESBL, XDR/PDR producing Escherichia coli and Klebsiella spp. continue to be a severe problems in renal transplant recipients.

<table>
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<th>Table 1. Urinary tract infections in renal transplant recipient</th>
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<tr>
<td>The most common causative agent</td>
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<td>Entrococcus spp</td>
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<td>Resistance Rates</td>
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<tr>
<td>Ciprofloxacin</td>
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<tr>
<td>trimethoprim/</td>
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<td>sulfamethoxazole</td>
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<td>ESBL</td>
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<td>XDR</td>
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<td>PDR</td>
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Note: E. coli and Klebsiella spp.

Figure 1. Urinary tract infections in renal transplant recipient in 2016-2021
Rasch Validation of the Psychosocial Assessment of Candidate Transplant Scale for Patients on Waitlist Deceased Donor Kidney Transplantation in South Korea

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Introduction: Psychosocial assessment of transplantation candidates is an integral part of transplantation evaluation that allows early detection of patients vulnerable to psychosocial issues during their difficult waitlist period. Particularly in Korea, psychosocial assessment of candidates is a critical issue for transplantation professionals, given recent serious social issues such as the ongoing decrease in organ donors and the long waiting time for deceased donor transplantation compared with Western countries. Therefore, pretransplant psychosocial evaluation is necessary to be suitable for transplantation. However, no validated global standardized psychosocial assessment tool for candidates on transplantation waitlists is currently available. Transplantation professionals are having particular difficulties in managing kidney transplantation candidates, who form the largest group of organ candidates and experience the longest waiting times, and in identifying those who are eligible to receive a kidney. The Psychosocial Assessment of Candidates for Transplantation scale can be completed more quickly, improved clinical ease of use, shown good inter-rater reliability, and is a uniform framework for pre-transplant evaluation across all organ systems. Moreover, this tool fit Korean cultural circumstance. However, there is no validation study of this instrument among transplantation patients.

Methods: The study aimed to conduct a Rasch Item Response Theory analysis of the Psychosocial Assessment of Candidates for Transplantation scale to evaluate the validity and utility of the tool in Korean transplantation clinical practice. In a transplantation center in South Korea, 157 deceased donor kidney transplantation candidates on the waitlist were subjected to Rasch analysis using Stata. Each of eight 5-point Likert scales was categorized as a binary variable using a 3 cut-off.

Results: All the dichotomously categorized items fit the Rasch model. R1c statistic and Anderson test results showed that the model fit was stable (p>.05), and both outfit and infit statistics were between -1.94 and 1.07. The estimate of the item discrimination parameter was 1.416. Item difficulty was between -0.22 and 2.27, reflecting acceptable and good levels.

Conclusions: Rasch analysis is a rigorous evaluation of the tool to more objectively assess the psychosocial evaluation in a clinical setting. The strengths of the present study are that this scale was shown to have good item validity by using Rasch analysis’s ability to exclude the bias caused by the target population’s differing scale-response abilities and unique cultural characteristics. The findings indicate that this scale has the item properties of an effective screening instrument and is clinically useful as a valid psychosocial assessment tool for Korean kidney transplantation candidates.

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Abstracts

P8.096
Adaptation Process After Kidney Transplantation in Korean Elderly Recipients: A Qualitative Study

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Introduction: Worldwide, the number of patients with chronic kidney disease is steadily increasing result of the aging population. Especially, South Korea is becoming the most rapidly aging society in the world. Nowadays, age is not an absolute contraindication to kidney transplantation caused by the improved surgical techniques and the developed immunosuppressants related to kidney transplantation. For this reason, there is an increase in elderly patients receiving kidney transplants globally including in Korea. However, they are who elderly kidney transplantation recipients still have many risk factors basically according to age. In other words, elderly kidney transplant recipients may be facing many challenges and susceptible circumstances. As a result, elderly recipients may experience an adaptation process after kidney transplantation different from other adult kidney transplant recipients.

Methods: This study aimed to explore the process of adaptation after kidney transplantation in elderly recipients. A qualitative descriptive design was used based on the grounded theory methodology developed by Strauss and Corbin. Data were collected through individual in-depth interviews with individual participants. Qualitative data from transcribed notes and field notes were analyzed using constants comparative method with theoretical saturation.

Results: A total of 16 elderly kidney transplantation (≥ 60 years) were recruited at a university hospital in South Korea. The core category of adaptation process after kidney transplantation in elderly recipients was ‘A journey of straining to save the last lifeline’. The adaptation process consisted of three stages ‘Confusing stage’, ‘Depressed stage’, and ‘Compromising stage’. Causal condition was ‘Unexpected reality with multiple restriction’ and contextual conditions were ‘Support system’ and ‘Medical resources’. The action/interaction strategies were ‘Practicing self-management’, ‘Appreciating and expecting’, ‘Holding will to live’, and ‘Accepting reality’. The consequences were ‘Acclimatization’ and ‘Withdrawal’.

Conclusion: Although the number of kidney transplantation in the elderly is increasing associated with a many advantages of quality of life, survival, they experience some of difficulties after transplantation and face an unexpected crisis. That is, the experience and adaptation process after kidney transplantation in elderly recipients is different from those of other adult kidney recipients. Therefore, tailored interventions based on an in-depth understanding of the adaptation process found in this study are needed to improve adaptation after kidney transplantation in elderly recipients. In particular, feasible and realistic education and counseling are required for each adaptation phase, considering that adaptation occurs in a long period adaptation after transplantation.

This manuscript is based on a part of the first author’s doctoral dissertation from Jeonbuk National University. We also thank Mr. Jon S. Mann of UIC for his editorial support.
Introduction: People on the kidney waitlist are counselled on expected waiting time, but are less informed about their waitlist experience, including temporary or permanent removal from waitlist (i.e. delisted). Disparities may exist in who is delisted. We aimed to describe and evaluate factors associated with the patient journey after entering the waitlist for deceased donor kidney transplant regardless of whether they were transplanted or not.

Method: We included all incident patients waitlisted for their first kidney transplant from deceased donor in Australia between 1st Jul 2006 and 31st Dec 2019. We described all clinical transitions after entering the kidney waitlist including: active on waitlist; delisted; kidney transplant; graft failure; death and censored (Fig 1). We summarized the median time to each transition until first transplant and annual percentages in each clinical state until 5 years. We used multi-state Markov model to evaluate factors associated with transitions after entering the waitlist until first transplant, reporting the hazard ratio (HR) for each transition.

Results: 8,466 people entered the kidney waitlist where 6,741 people received their first transplant (6,163 deceased donor; 506 living donor; 99 paired kidney exchange donor), 381 people died while waiting (31 active on waitlist; 350 delisted) and 1,344 were still waiting for a transplant (844 active on waitlist; 500 delisted) by the end of follow-up. Nearly two-thirds (63%) were never delisted while waiting, but 2,111 (25%) were delisted once and 1,016 (12%) were delisted ≥2 times. Of those delisted, 47% spent a total of <6 months off-waitlist. Median time from waitlist to transplant increased with number of times delisted, from 4.8 months (IQR:1.7 months-1.2 years) in patients never delisted to 3.2 years (IQR:2.1-4.6 years) in patients delisted ≥2 times. At 1-year, the probability of transplant was 41% (95%CI:40-42%), active on waitlist was 42% (95%CI:41-43%), delisted was 11% (95%CI:10-12%) and death was 1.4% (95%CI:1.2-1.7%) (Fig 2). At 5-years, this increased to 63% (95%CI:62-64%) transplanted, 5% (95%CI:4-5%) active on waitlist, 10% (95%CI:9-11%) delisted and 13% (95%CI:12-14%) died.

Factors associated with increased likeliness of transitioning from active to delisted included age at waitlist entry (≤29 years: 1.21HR, 95%CI:1.09-1.35; ≥65 years: 1.15HR, 95%CI:1.04-1.27), more recent year of commencing dialysis (2016-19: 1.34HR, 95%CI:1.22-1.47), AB blood group (1.26HR, 95%CI:1.02-1.55), delisted more than once (1.63HR, 95%CI:1.52-1.76), and cause of kidney failure (diabetes: 1.38HR, 95%CI:1.26-1.50).

Conclusion: The patient experience on transplant waiting list was not straightforward, where about one-third of patients were delisted at least once and had longer time to transplant. Our findings will aid in counselling patients and further support in younger patients may benefit their return to waitlist.
Surveying the Quality of Life and Its Dimensions Among Kidney Recipient Patients Referred to the Sina Organ Procurement Unit in 2021

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Introduction: The quality of life (QOL) is considered as one of the most important methods for evaluation of treatment and care. In this regard, the aim of this study was to identify the quality of life and its dimensions and the relational pattern between demographic characteristic and dimensions of QOL.

Method: The sample consisted of 94 patients who kidney transplanted from cadaveric donation referred to Sina hospital of Tehran university of medical sciences. Subjects answered 2 section questionnaires: (1) Demographic characteristic, (2) Standard instrument of QOL related to health (SF36) contains 36 questions that assess eight aspects of health quality of life: physical functioning, role-physical functioning, bodily pain, general health, vitality, social functioning, role-emotional functioning, and mental health. All data collected by one trained transplant coordinator who worked directly with these patients. The data were analyzed by descriptive statistics and inferential statistics (ANOVA, T test, chi square, and linear regression).

Result: From the total numbers of patients, 27 (28.7%) were female, 78(83%) were married, 34(36.2%) were under diploma and 32(34%) were freelance worker. The mean and SD were showed in Table 1. Significant differences between men and women were found for quality of life scores. The results showed that sex, level of education were meaningful relationship with QOL. The mean of QOL in participation were undesirable.

Conclusion: Almost half of kidney recipients were not have acceptable quality of life all dimensions, it is suggested that follow up and management should take care of bio- psycho- social support in transplantation patients for improving quality of life in this patients.

<table>
<thead>
<tr>
<th>Table 1: Demographic variables of participants</th>
<th>(Mean ±SD) , Median</th>
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<tbody>
<tr>
<td>Age</td>
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<tr>
<td>Gender</td>
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</table>
Post-operative Myocardial Infarction After Renal Transplant: Setback or Disaster?
Joanne Devlin1,2, Karen Stevenson1, David Kingsmore1,2, John Asher1,2.
1Renal and Transplant Surgery, Queen Elizabeth University Hospital, NHSGGC, Glasgow, United Kingdom; 2ICAMS, University of Glasgow, Glasgow, United Kingdom.

Introduction: There is controversy surrounding the role of pre-operative cardiovascular screening for potential transplant candidates. Postoperative myocardial infarctions (MI) are wide ranging in their clinical picture, and a balance is needed between the risk of post operative MI against delayed listing or denial of transplant.

Methods: We retrospectively reviewed all adult renal transplant recipients in our centre from 2010 to 2021 to identify patients with MI within 30 days following transplant, based on a diagnosis of an MI in the electronic record, an MI mentioned on the patient discharge letter, or a Troponin I level of 35 or more with a 20% change (from the Fourth Universal Definition of an MI (2018)). We reviewed the patients who had an MI, including past medical history, medications, and pre-operative cardiac investigations.

Results: Of the 1627 adult transplant recipients over the 11-year period there were 27 patients who had a post-operative MI. 18 patients were male (67%) and 9 patients were female (33%). The mean age of the patients with an MI was 61.5 years, with a median age of 61 years and minimum of 45. 8 patients were diabetic (30%). Comparing patients over 45, 1-year patient survival was noted to be 96% both in the MI group and the non-MI group, while 5-year patient survival was 68% vs 83%. 5-year uncensored graft survival, including deaths with functioning graft, was 68% vs 74% for recipients without MI.

Conclusions: Post-operative MI occurred in 1.6% of transplant recipients but was not associated with significantly reduced 1 year or 5 year patient survival post transplant suggesting that current cardiovascular assessment for transplant results in satisfactory cardiac outcomes post transplant and the risks from delayed listing should be weighed against perceived benefits of asymptomatic screening. Further work is needed to elucidate MACE outcomes in the assessed but non waitlisted population.

Transplant in Times of the Beginning of SARS-COV2 Pandemic, Experience in Reference Center Public Hospital in Mexico
Luis Garcia1,2, Flor Rojas1, Perez Karina1, Diana Fernandez1, Aldo Garcia1, Hector Hinojosa1, Lionel Vargas1.
1Surgery, Hospital General de Mexico Dr. Eduardo Liceaga, Ciudad de Mexico, Mexico; 2Surgery, Hospital Especialidades CMN SXXI IMSS, Ciudad de Mexico, Mexico.

Introduction: The new coronavirus disease 2019 (COVID-19) had an impact on the health system worldwide after being declared a pandemic, causing the stoppage of solid organ transplants in various countries. In Mexico, once the pandemic was declared, the National Transplant Center for government proclaimed the cessation of activities at the national level, continuing for the following 6 months.

Materials and Methods: Retrospective cohort, included transplant patients at Hospital General de Mexico, from January 2020 to January 2021, with follow-up for a period of 3 months. Descriptive statistics were performed.

Results: 9 patients with deceased donor Kidney Transplant were included, mean age 31.32 ± 7.8 years, 60% male, the main cause of Kidney Disease was undetermined in 77.7%, one of glomerulate basal membrane, and one with nodular diabetic glomerulosclerosis. One patient with preformed DQ7 ADEs, all receive induction with Thymglobulin, and maintenance with triple scheme. During the follow-up there was one hyper acute rejection secondary to non-HLA humoral rejection plus venous thrombosis due to protein S deficiency, a second patient presented an event of acute kidney injury AKIN3, secondary to gastroenteritis due to C. difficile, with complete recovery, the 3rd patient presented Hypovolemic shock, secondary to sub aponeurotic hematoma. 44.4% of patients presented delayed graft function, with stable renal function during follow-up.

Conclusion: During the pandemic, kidney transplantation was safe in our center, compared to keeping patients with replacement therapy with improvement in quality of life and mortality. No cases of receptors with COVID-19 disease was found.
Is Pregnancy Possible in Kidney Transplant Patients? Experience in a Reference Center in Mexico

Luis Garcia1,2, Karina Perez3, Flor Rojas3, Diana Fernandez1, Aldo Garcia1, Hector Hinojosa3, Lionel Vargas3.
1Surgery, Hospital General de Mexico Dr. Eduardo Liceaga, Ciudad de Mexico, Mexico; 2Surgery, Hospital Especialidades CMN SXXI IMSS, Ciudad de Mexico, Mexico; 3Nephrology, Hospital General de Mexico Dr. Eduardo Liceaga, Ciudad de Mexico, Mexico.

Background: The risk of complications during pregnancy is higher in women with CKD compared to healthy women, with a 10-fold increased risk for the development of preeclampsia, 5 times higher for the development of preterm labor and low birth weight, and 3 times the risk of termination of cesarean delivery. A recovery of fertility 6 months after transplantation has been observed in transplanted women.

Objective: To know the incidence of patients with pregnancy after kidney transplantation in our center, as well as the outcomes.

Methodology: A series of consecutive cases of post-transplanted women, over 18 years of age in our center from January 1, 2012 to January 1, 2020, who had at least one initial assessment at the time of pregnancy and a follow-up of at least 6 months, with adequate graft function at the time of pregnancy with adequate function of the graft at the time of pregnancy with its outcomes after the end of it. Data were collected retrospectively from their clinical record. Exclusion criteria: Patient with pregnancy prior to kidney transplantation, or whose follow-up is less than 6 months.

Results: We included 10 patients with chronic kidney disease and kidney transplantation, average age of 31.1±4.5 years, transplant interval of 5.98±2.2 years, most received renal graft from a living donor, the main induction therapy was with Basiliximab. Maintenance therapy during pregnancy in 83.3% was modified to tacrolimus, azathioprine and prednisone, and in one patient presented with consumption of tacrolimus, mycophenolate and prednisone, which was one of the pregnant losses that occurred. 50% received prenatal consultation and pre-pregnancy counseling, considered as planned pregnancies; in 1 patient there was deterioration of renal function with graft dysfunction, without improvement after the end of pregnancy.

Discussion: Most women with kidney transplantation can carry a pregnancy to term with excellent results, although adverse events are common. Rates of preeclampsia, induction, and cesarean section were significantly higher compared to the general population. Most of the patients were able to be followed up for a period longer than 5 years, observing impairment of graft function in 40% of patients who presented pregnancy, 30% of these with return to renal function replacement therapy.

Conclusions: Pregnancy in transplant patients from our hospital does not differ from that reported in the literature; our cohort is limited, however it is considered of great importance to increase the number of studies of this type in our country and thus be able to improve strategies to obtain better maternal and fetal results throughout the post-transplant.
P8.102

Teratoma in Transplanted Patient, Case Report and Review

Luis Garcia1,2, Lionel Vargas1, Diana Fernandez1, Dario Cantu1, Sandra Gutierrez1, Karla Manrique1, Aldo Garcia1, Lourdes Quintero3.
1Surgery, Hospital General de Mexico Dr. Eduardo Liceaga, Ciudad de Mexico, Mexico; 2Surgery, Hospital Especialidades CMN SXXI IMSS, Ciudad de Mexico, Mexico; 3Pathology, Hospital General de Mexico Dr. Eduardo Liceaga, Ciudad de Mexico, Mexico.

Background: Compared with the general population, a transplant patient has a 10-fold higher incidence of developing a de novo neoplasm. Added to the common factors of the general population are immunosuppression, or the existence of oncoviruses.

Methodology: We describe the case of a 59-year-old male, group B+, who received a transplant from a Related Living Donor in 2011, sharing a haplotype, undergoing induction with Daclizumab 80mg DU, and with immunosuppression based on Cyclosporine 1.8mg every 12h, Mycophenolate 1g every 12 hours and Prednisone 5mg every 24 hours; He began suffering in December 2020 with abdominal pain in the epigastrium, hypotension and weight loss, Laboratories: Creatinine: 1.15, Urea 32, Glucose 102mg/ dL, Hb 17.6mg/ dL, Hto 52.40, Leukocytes 7.9X1000, Platelets 233x1000; tumor markers: Alpha fetus 2.16 ng/ml, CA 19-9 524.5 IU/ml, A. Carcinoembryonic 67.53 ng/ml. On examination, the kidney graft showed no alterations, and a palpable abdominal tumor of 30 x 25 cm, painful on palpation. Tomography reported a retroperitoneal tumor of 25.8 x 16.9 x 19 cm with displacement of adjacent structures and compression of the inferior vena cava.

Resection of the tumor is performed, finding: Retroperitoneal tumor of 25 x 25 x 20 cm on the vena cava and aorta, which displaces the pancreas towards the head, without its involvement, with a mucous content of 2 Lts.

At one month of follow-up with creatinine 0.94, Hb 12.2, Hct 36.4, plaq. 284, leukocytes 6.0. With tolerance to the oral route, without pain, and definitive histological report compatible with Retroperitoneal Mature Teratoma.

Discussion: Primary mature teratomas are rare nonseminomatous germ cell tumors of well-differentiated parenchymal tissues composed of somatic cell types, more common in childhood and rarely in adults where it represents 1 to 11% of retroperitoneal tumors, more frequently in women in a 3:1 ratio and are usually located near the upper pole of the kidney, more frequently on the left side, or in structures in midline. Retroperitoneal teratomas represent only 4% of all primary teratomas. Only a few case reports have been documented in the literature. Serum markers, such as CA19.9, CEA and AFP, may be elevated. The rate of malignancy in adults is 26% and increases with age, male sex, and the presence of immature tissues and solid components. Surgical resection is the mainstay in the treatment. Although mature teratomas are benign, malignant transformation occurs in 3-6%. The prognosis after complete resection has a five-year survival rate of 100%.

Conclusions: Mature primary retroperitoneal teratomas very rarely occur in adult male patients and are usually asymptomatic. The definitive diagnosis is established after histological evaluation. Surgical resection is the main treatment to evaluate if there are immature and solid elements that need long-term follow-up due to the increased risk of malignancy.
Main Clinical Outcomes in Living-Donor Kidney Transplantation: A Latin-American Cohort

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1Bogota D.C, Colombiana de Trasplantes, Bogota, Colombia.

Background: Living donor kidney transplant (LDKT) is one of the best therapeutic options for end-stage kidney disease (ESKD). The graft and patient survival rates are significantly higher in living-donor kidney transplantation (LDKT) compared to deceased-donor kidney transplantation. However, there is a lack of information in Latin-American populations. Colombiana de Trasplantes has been one of the centers in Colombia that have performed a high proportion of kidney transplantation from living donors. Therefore, we aimed to evaluate main clinical outcomes, graft, and patient survival for LDKT at our center.

Methods: We retrospectively evaluated a total of 530 LDKT patients who underwent transplantation from August 2008 to August 2020 at Colombiana de Trasplantes. Graft survival censored for death and patient survival were determined up to 5 years post transplantation by the Kaplan-Meier method. Frequency of thrombosis, hematoma, urinary leak, and reoperation were documented.

Results: A total of 530 LDKT patients were analyzed. Most patients were male (56%). The predominant known chronic kidney disease etiology was glomerular (n = 163, 30.8%). There were 123 (23.2%) LDKT patients with a preemptive transplant. Dialysis duration was 22.1 ± 33.5 months. Most kidney recipients had a medical history of hypertension (n = 405, 76.4%). Besides, 43 LDKT patients were obese (8.1%). Most of the live kidney donors (LKD) were female (n = 279, 52.6%), and relatives for the recipient (n = 366, 69.1%). Main clinical outcomes were mortality (n = 22, 4.1%) and graft loss (n = 46, 8.6%). The graft survival death-censored rates were 93.7% and 89% at 1 and 5 years respectively. Patient survival rates were 97.0% and 94.1% at 1 and 5 years respectively. During the follow-up period, a total of 13 patients had vascular complications (2.4%), 18 had peri transplant hematoma (3.4%), 48 had urinary leak (9.1%), and 98 required reoperations (18.5%).

Conclusion: This study describes the experience of 5 years performing LDKT. Long-term graft and patient survival rates in our center are comparable to prior reports from other leading centers. Since there have been many updates in the field of transplantation, clinical outcomes from a medium-sized center can be noteworthy, although not entirely new.
Main Outcomes of Pediatric Living Donor Kidney Transplantation: A Latin-American Cohort
Yenny Baez Suarez1, Andrea Garcia Lopez1, Nasly Patiño Jaramillo1, Fernando Giron Luque1.
1Bogota D.C, Colombiana de Trasplantes, Bogota, Colombia.

Background: Renal transplantation in children reduced mortality, improved growth potential, cognitive development, and quality of life. Nevertheless, kidney transplantation in children remains a challenge because of their small size and the scarcity of appropriate allografts. Living-donor kidney transplantation (LDKT) offers higher graft and patient survival rates, and fewer complications compared with transplantation of deceased donors. However, there is a lack of information in Latin-American pediatric kidney transplant patients. Colombiana de Trasplantes has been one of the centers in Colombia that have performed a high proportion of pediatric kidney transplantation from living donors. Therefore, we aimed to evaluate main clinical outcomes, graft, and patient survival for LDKT at our center.

Methods: We retrospectively evaluated a total of 67 LDKT pediatric patients who underwent transplantation from August 2008 to August 2020 at Colombiana de Trasplantes. Graft survival censored for death and patient survival were determined up to 5 years post transplantation by the Kaplan-Meier method. Frequency of thrombosis, hematoma, urinary leak, and reoperation were documented.

Results: A total of 67 LDKT patients were analyzed. Most patients were male (55.2%). The predominant known chronic kidney disease etiology was congenital (n = 24, 35.8%). There were 14 (20.9%) LDKT patients with a preemptive transplant. Dialysis duration was 9.2 ± 13.9 months. Most of the live kidney donors (LKD) were female (n = 39, 58.2%), and relatives for the recipient (n = 61, 91%). Main clinical outcomes were mortality (n = 1, 1.5%) and graft loss (n = 14, 20.9%). The graft survival death-censored rates were 83.2% and 78.8% at 1 and 5 years respectively. Patient survival rates were 98.4% at 1 year and were constant during the follow-up. During the follow-up period, a total of 6 patients had vascular complications (8.9%), 1 had peri-transplant hematoma (1.5%), 7 had urinary leak (10.4%), and 17 required reoperations (25.4%).

Conclusion: This study describes the experience of 5 years performing LDKT. Our program of pediatric kidney transplantation has achieved optimal patient and graft survival rates with low rate of complications. Since there have been many updates in the field of transplantation, clinical outcomes from a medium-sized center can be noteworthy, although not entirely new.
P8.105

Risk Factors for Urologic Complications After Kidney Transplantation and Impact in Graft Survival

Laura Niño Torres¹, Andrea Garcia Lopez¹, Nasyly Patiño Jaramillo¹, Fernando Giron Luque¹, Alejandro Niño Murcia¹.
¹Bogota D.C, Colombiana de Trasplantes, Bogota, Colombia.

Introduction: Kidney transplantation (KT) is the best therapy for chronic kidney disease (CKD). The second most common etiology associated with morbidity and graft loss after KT are major urologic complications (MUCs). The advancement and modifications of surgical techniques have prevented MUCs. The objective of this study is to estimate the incidence, risk factors, and impact on graft survival associated with urological complications in KT patients.

Methods: A retrospective cohort was obtained by electronic records of kidney transplant recipients operated in Colombiana de Trasplantes for the period between August 2008 to September 2019. Initiation of follow-up was defined as the date of transplantation up to 3 years post-transplantation. Incidence of ureteral stenosis, ureteral obstruction, and ureteral leak was measured. A logistic regression multivariate model was adjusted to determine the associated factors to MUCs (yes/no). Patient and graft survival time were analyzed using a Kaplan-Meier methods.

Results: A total of 1584 KT patients were analyzed during the study period. MUCs were present in 195 (12.6%) of the KT patients. Dialysis duration, cold ischemia time, and operation room time (ORT) were significant in the bivariate analysis. A multivariate analysis indicated that dialysis duration and cold ischemia time remained significant for the incidence of MUCs. Probability of graft and patient survival at 3 years of follow-up was 90.5% and 85.5% respectively. No significant difference was found on graft and patient survival in KT patients with or without MUCs.

Conclusion: MUCs are frequent complications for KT and represent an important burden for the patient and the health system. Our study has shown no significant difference in graft or patient survival. The identification of MUCs and risk factors may guide transplant teams for future surgical and clinical decisions.

<table>
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<th>Table 1. Recipient baseline characteristics, intraoperative findings, and frequency of MUCs after KT</th>
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<tbody>
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<td>Recipient characteristics</td>
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<tr>
<td>---------------------------</td>
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<tr>
<td>Gender, n(%)</td>
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<tr>
<td>Age, groups (%)</td>
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<tr>
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<tr>
<td>18-49</td>
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<td>Obstructive</td>
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<tr>
<td>Recurrent urinary tract infection</td>
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<tr>
<td>Ureteral stricture</td>
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<td>Dystrophy type, n(%)</td>
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<tr>
<td>Peritoneal dialysis</td>
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<tr>
<td>Pre dialysis (percutaneous transplant)</td>
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<tr>
<td>Dystrophy duration (months), mean (SD)</td>
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<td>Anemia, n(%)</td>
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<tr>
<td>Diabetes, n(%)</td>
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<td>BMI (kg/m²), mean (SD)</td>
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<td>18-35</td>
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<td>Cold ischemia time (hours), mean (SD)</td>
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<td>Warm ischemia time (min), mean (SD)</td>
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<td>Other</td>
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<td>ORT (hours), mean (SD)</td>
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<tr>
<td>Interspersive Double J stent, n(%)</td>
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<tr>
<td>Cystitestasis, n(%)</td>
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<td>Interspersive complications, n(%)</td>
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</table>

SD: standard deviation; CKD: Chronic Kidney Disease; BMI: Body Mass Index; ORT: Operation Room Time. Variables with missing data: *Dystrophy type (1), *Dystrophy duration (4), *Anemia (5), *BMI (6), *ORT (1). *Variables with p<0.05 are included in the multivariate analysis.
Comparison of Three Glomerular Filtration Rate Estimating Equations With 24-Hour Urine Creatinine Clearance Measurement in Live Kidney Donors

Fernando Giron Luque1, Andrea Garcia Lopez1, Nasly Patiño Jaramillo2, Bogota D.C, Colombiana de Trasplantes, Bogota, Colombia.

Background: It is very important to determine as accurately as possible the renal function in potential living kidney donors (PLKD). The direct measurement of glomerular filtration rate (mGFR) has been considered the “gold standard” for the kidney failure evaluation. Nonetheless, these are not available in many medical centers due to the complexity of the technique. The estimated GFR with 24-hour urinary creatinine clearance (CICr) is frequently used because of its availability. In this study we aim to compare the different eGFR using serum-based creatinine formulas (Cockcroft-Gault, MDRD and CKD-EPI) and the eGFR based on 24-hour urinary creatinine clearance to determine the usefulness of eGFR creatinine formulas to evaluate kidney function in PLKD.

Methods: We evaluate kidney function in 799 PLKD using 24-hour urinary CICr method. The GFR obtained was compared with eGFR based on creatinine (Cockcroft-Gault, MDRD and CKD-EPI). We calculated mean bias (difference), precision (SD of this difference), accuracy (proportion of eGFR within ±10% of ClCr GFR) and performed Bland-Altman-plots.

Results: Using the Bland Altman graphic, we observed that the most dispersed results are obtained using MDRD. Smallest mean bias was observed for Cockcroft-Gault (bias of 5.8; SD 25.1) compared to the other equations (CKD-EPI: bias of 9.8; SD 24.8 and MDRD: bias of 13.8; SD 25.3). Smallest bias was found in females for the three equations. Results of mean bias were similar when comparing the three equations in patients with ClCr GFR < 60, however, smaller mean bias were found for the three equations above age 40 years. Regarding the assessment of the 95% limits of agreement -43.4 (Cock-roft-Gault). The interval range was too high to assume equivalence between 24-hour urinary ClCr method and eGFR highest upper limit of agreement 63.5 (MDRD) and the highest lower limit of agreement -63.5 (MDRD) and the highest lower limit of agreement -63.4 (Cock-roft-Gault).

Conclusion: In this PLKD cohort, Cockcroft-Gault equation showed the highest approximation to the reference method. The interval range was too big to assume equivalence between 24-hour urinary ClCr method and eGFR based on creatinine (Cockcroft-Gault, MDRD and CKD-EPI).

Predicting 5-Year Survival After Kidney Transplantation in Colombia

Laura Niño Torres1, Andrea Garcia Lopez2, Nasly Patiño Jaramillo2, Fernando Giron Luque1, Alejandro Nino-Murcia MD1.
1Department of Transplant Surgery, Colombiana de Trasplantes, Bogota, Colombia; 2Department of Transplant Research, Colombiana de Trasplantes, Bogota, Colombia.

Introduction: Kidney transplantation is the gold standard treatment for end stage kidney disease (ESKD) with a significant impact on morbidity and mortality. Given organ shortages and limited resources it is important to focus on improving graft and patient survival. Post-transplant success is influenced by a complex relationship between donor and recipient characteristics which necessitated the development of a tool to individualize decision-making for clinical kidney offers. Survival benefit is estimated by comparing the predictive survival of the patient with transplantation versus the predictive survival of remaining on the waiting list. It involves two previous indexes, the Kidney Donor Profile Index (KDPI) which focused on the kidney graft quality and the Estimated Post Transplant Survival (EPTS) which evaluates the recipient. This tool was developed in the United States and was used it to evaluate the predicting survival benefit after deceased-donor kidney transplantation in Colombia.

Method: Retrospective historic cohort study which included all the adult deceased-donor kidney transplant patients between January 2009 and December 2021. A descriptive analysis of clinical and sociodemographic characteristics, including KDPI and EPTS was performed. The online tool was used to calculate the estimated-5 year predicting survival benefit for each patient. This will later be compared to graft survival and patient mortality for our population.

Results: Out of 1235 kidney transplant patients in the period evaluated, 1145 patients had complete information (92.7%). 60.3% were male, with a mean age of 46.2 years (± 12.6). 17.1% were diabetic and had been in dialysis for 44.8 months (±44.0). Diabetic chronic kidney disease etiology as unknown for 35.3%. Donors were 42.7 years old (±15), predominantly male (60.8%), and average BMI of 25.5 kg/m² (±4.98). 75.5% were non-diabetic and 96.2% were non-diabetic, with cerebrovascular disease as cause of death (50.5%), mean creatinine was 0.98 mg/dl (±0.45). KDPI was 44.9% (±27.9%), 60.2% in between 20 and 80%. Predictive survival for patients if they were to remain waitlisted for 5 years was 70.6%, if they were to receive the transplant was of 89.3%, which results in a survival benefit of 18.7% for our population. Graft survival at 5 years was 72.7% and patient survival was 86.3%.

Conclusion: Survival benefit for patients with ESKD has been well documented in literature. Nevertheless, this study reflects the survival benefit for our specific population in Colombia, regarding both donor and recipient characteristics. This tool may be crucial for patient counseling and physician decision making patient tailored.
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<tr>
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<th>Total (N=5145)</th>
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<tbody>
<tr>
<td>Sex, n (%)</td>
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<tr>
<td>Female</td>
<td>452 (39.5%)</td>
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<tr>
<td>Male</td>
<td>693 (60.5%)</td>
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<tr>
<td>Age years, mean (SD)</td>
<td>46.2 (12.8)</td>
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<tr>
<td>Diabetes, n (%)</td>
<td>196 (17.1%)</td>
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<td>Dialysis time months, mean (SD)</td>
<td>44.8 (44.0)</td>
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<td>Dialysis type, n (%)</td>
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<tr>
<td>Hemodialysis</td>
<td>667 (58.3%)</td>
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<td>Peritoneal</td>
<td>430 (37.6%)</td>
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<td>Predialysis (preemptive transplant)</td>
<td>48 (4.2%)</td>
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<th>Number of previous organ transplants, n (%)</th>
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<tr>
<th>EPTS, mean (SD)</th>
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<tr>
<td>29.1% (24.1%)</td>
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<th>EPTS, n (%)</th>
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<tr>
<td>&lt;20</td>
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<td>20-80</td>
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<td>&gt;80</td>
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<th>Underlying cause of CKD, n (%)</th>
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<td>Obstructive</td>
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<th>Donor characteristics</th>
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<td>Donor age, [years] mean (SD)</td>
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<td>Female</td>
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<tr>
<td>Male</td>
</tr>
<tr>
<td>BMI</td>
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<table>
<thead>
<tr>
<th>History of Hypertension, n (%)</th>
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<tbody>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>yes, 0-5 years</td>
</tr>
<tr>
<td>yes, 6-10 years</td>
</tr>
<tr>
<td>yes, &gt; 10 years</td>
</tr>
<tr>
<td>yes, unknown duration</td>
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<table>
<thead>
<tr>
<th>History of Diabetes, n (%)</th>
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<tr>
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<tr>
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<tr>
<td>yes, 0-5 years</td>
</tr>
<tr>
<td>yes, &gt; 10 years</td>
</tr>
<tr>
<td>yes, unknown duration</td>
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<tr>
<th>Cause of Death, n (%)</th>
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<tbody>
<tr>
<td>Cerebrovascular/stroke</td>
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<tr>
<td>Anoxia</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Head trauma</td>
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<tr>
<td>SNCTumor</td>
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<table>
<thead>
<tr>
<th>Serum Creatinine (mg/dL)</th>
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</thead>
<tbody>
<tr>
<td>0.980 (0.445)</td>
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</table>

<table>
<thead>
<tr>
<th>KDPI, mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>44.9% (27.9%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>KDPI, n (%)</th>
</tr>
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<tbody>
<tr>
<td>&lt;20</td>
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<tr>
<td>20-80</td>
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<tr>
<td>&gt;80</td>
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<table>
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<tr>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Waiting list survival</td>
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<tr>
<td>Kidney transplant survival</td>
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<tr>
<td>Survival benefit</td>
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</tbody>
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<td>B</td>
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Focal segmental glomerular sclerosis (FSGS) is the most common glomerular disease leading to end-stage renal disease (ESRD) in children. FSGS frequently recurs after kidney transplant and may cause graft failure. Therapeutic plasma exchange (TPE), rituximab and steroids have been used to treat post-transplant FSGS recurrence, but limited data is available to support their combined efficacy. We conducted a retrospective cohort study of all kidney transplant recipients at a single pediatric center between 2007 and 2018 to determine frequency of FSGS and early recurrence of nephrotic syndrome within 4 days of transplant. Primary outcome was graft survival and secondary outcome was remission of nephrotic syndrome.

FSGS was the indication for renal transplant in 11% of cases (n=29). Of these, 24% of patients had early FSGS recurrence after transplant (n=7). Treatment was at the discretion of the treating physician, but generally included TPE, rituximab and steroids. Five responded; the other two returned to chronic dialysis. 22 patients without recurrence experienced 100% 1-year graft survival. For all FSGS recipients, including those with recurrence, 3-year graft survival was 94.4%. 5/7 (71%) of recipients with recurrence achieved partial remission of nephrotic syndrome following treatment.

This study, the largest to uniformly employ the combination of TPE, rituximab and high-dose steroids, supports the efficacy of this treatment for pediatric patients with FSGS recurrence.

Simultaneous Vascular and Antibody-Mediated Rejection (AMR) in Pediatric Patients Caused Poor Prognosis in Renal Allograft

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Introduction: The prognostic significance of simultaneous vascular rejection (VR) and AMR on graft survival is not clear enough, especially in the pediatric population. Accordingly, this study aims to determine the impact of simultaneous VR and AMR on the development of transplant glomerulopathy (TG) and interstitial fibrosis (IF) with the resulting graft survival.

Methods: Forty-five recipients younger than 18 were separated into Group 1 patients (n=25) with pure AMR and Group 2 patients (n=20) with simultaneous VR+AMR. Tubular expression of TNF-α, TGF-β, and HLA-DR was evaluated. Peritubular capillary (PTC) and interstitial leukocytes were highlighted with TNG-α, HLA-DR, and CD68. The loss of HLA-DR expression on PTCs was studied to determine the PTC destruction. Diffuse IF and TG development were analyzed in the follow-up biopsies.

Results: The response of Group 2 patients to rejection therapy was lower than Group 1 patients (p<0.001). PTC C4d expression was found higher in Group 2 than Group 1 (P<0.001). Group 2 showed a higher PTC destruction, IF, and TG incidence than Group 1 (P<0.001). The development of IF and TG increases with the increasing degree of glomerulitis, C4d expression, and PTC destruction (p<0.01). Tubular and interstitial TNF-α, TGF-β, and HLA-DR expressions were found higher in Group 2 compared to Group 1 (p<0.01). The degree of PTC destruction and C4d expression increased with increasing leukocyte and macrophage infiltration in PTCs and interstitium (p<0.01). The development of IF and TG decreased with increasing intensity of PTC and interstitial infiltration, glomerulitis, PTC destruction, and C4d expression (p<0.01). Also, the development of IF and TG shortened with increasing HLA-DR, TNF-α expression in inflammatory cells and increasing TNF-α, TGF-β, HLA-DR expression in tubular cells (P<0.01). Overall, the 1-, 3-, and 5-year graft survival was 96%, 92%, and 79%, respectively, for Group 1 patients, while 96%, 40%, and 10% respectively for Group 2 recipients (p<0.001).

Conclusion: The prognosis and course of antibody-mediated vascular rejection are noticeably different from pure AMR, with antibody-mediated vascular rejection having the poorest outcome through leading the early development of IF and TG via augmenting inflammatory and fibrotic pathways. Thus, developing new treatment strategies for antibody-mediated vascular rejection could salvage many kidney allografts.
The Beneficial Impact of D3 Vitamin on the Decline of Rejection, Epithelial-Mesenchymal Transition (EMT), And Interstitial Fibrosis Among Pediatric Renal Transplant Patients

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Introduction: Vitamin D3 is known to prevent T-cell proliferation and inhibit the production of TNF-α. Vitamin D3 also has a critical role in reorganizing the cytoskeletal of the cells and E-cadherin (Ecad) expression necessary for maintaining the epithelial state. Ecad downregulation is considered a hallmark of EMT. We aimed to understand the role of D3 in the development of acute rejection (AR), EMT, and interstitial fibrosis (IF).

Method: Of 51 cases, 24 were treated with D3 (Group D), and 27 did not (Group C). The intensity of interstitial macrophage and lymphocyte infiltration graded in the first indication biopsies. The α-SMA and paxillin expression on tubules were evaluated to detect EMT development. Additionally, tubular TGF-β, TNF-α, and Ecad expression were studied. Follow-up biopsies were analyzed for the development of AR during 18 and 24 months after transplant.

Results: The development of AR and IF during 18 and 24 months after transplant was found lower in Group D patients compared to Group C patients (p<0.001). Patients in Group D showed higher degrees of tubular Ecad expression than Group C (p<0.001). Tubular, α-SMA, paxillin, TGF-β, and TFN-α were found significantly lower in Group D than Group A (p<0.001). Tubular α-SMA, paxillin, TNF-α, and TGF-β expression positively correlated with the IF development (p<0.001). The degree of inflammatory cells showed a positive correlation with the tubular α-SMA, paxillin, TNF-α, and TGF-β expression (p<0.001). The overall -5 and 10-year graft survival was 91% and 87% for Group D, 70% and 63% for Group C, respectively (p<0.05).

Conclusion: With increasing degree of inflammation, TNF-α and TGF-β, the activation of EMT and therefore the occurrence of IF was found higher in Group C cases who had increased α-SMA and paxillin expression with Ecad downregulation. Contrarily, patients in Group D had a lower incidence of AR, EMT, IF, and favorable graft prognosis. Thus, D3 therapy is beneficial in renal transplant patients with its antifibrotic and immune modulator properties.

Epstein-Barr Virus-Positive T-Cell Lymphoma Characterized by Intestinal Involvement With Multiple Perforation in an Adult Renal Allograft Recipient: Two Case Reports

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1Department of Pathology, Baskent University, Ankara, Turkey; 2Department of General Surgery, Division of Transplantation, Baskent University, Ankara, Turkey.

Introduction: Post-transplant lymphoproliferative disorder (PTLD) is a relatively common post-transplantation malignancy affecting as frequently as 10% of all solid organ recipients. Most PTLDs are of B cell origin with a common Epstein-Barr virus (EBV) association. T-cell PTLDs are much rarer and less frequently associated with EBV. Here we report two unusual cases of EBV-positive T cell lymphomas causing intestinal ulceration and perforation in adult renal transplant recipients.

Cases: The first case is a fifty-two-year-old male with renal allograft who developed cryptogenic end-stage liver failure and was accepted as a candidate for liver transplantation. Meanwhile, he was admitted with severe abdominal pain, which resulted from ileal perforation. Pathologic evaluation of the intestinal resection showed diffuse malignant lymphoid infiltration of the ileum, which was consistent with anaplastic large cell lymphoma (ALCL). The tumor was positive for the Epstein-Barr virus (EBV) genome. The second case is a forty-seven-year-old male renal allograft recipient who developed acute abdomen in the 8th year of his transplantation. Explorative surgery revealed diffuse intestine involvement and large bowel involvement with EBV positive NK/T cell lymphoma.

Conclusion: T and NK/T cell lymphomas are rare forms of PTLDs, which are infrequently associated with EBV. This extraordinary form of PTLD, which shows an unexpected clinic such as bowel involvement and perforation in a late post-transplant period and EBV positivity, represents a rare clinic entity.
P8.112

Pregnancy Outcomes in Kidney Transplant Recipients And Their Newborns

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1Department of Nephrology, Baskent University, Ankara, Turkey; 2Department of General Surgery, Division of Transplantation, Baskent University, Ankara, Turkey; 3Department of Obstetrics and Gynecology, Baskent University, Ankara, Turkey.

Introduction: Kidney transplantation is associated with improved reproductive function in female recipients compared to patients on dialysis. In our center, 15 kidney transplant recipient women gave birth after transplantation under close follow-up and regulation of immunosuppressive treatment prior to pregnancy. We aimed to describe the perspective of gestation and birth in female kidney transplant recipients in Baykent University in the last 10 years.

Materials & Methods: Fifteen female kidney transplant recipients who gave a birth between years 2012-2022 were included. Maternal and fetal complications are reported to be at higher rates in kidney transplant recipients. Cessation of mycophenolate mofetil/mycophenolate sodium and conversion to azathioprine and ongoing calcineurin inhibitors is the protocol of prior to pregnancy. We aimed to describe the perspective of gestation and birth in female kidney transplant recipients in our center, 15 kidney transplant recipient women gave birth after transplantation.

Results: Pregnant kidney transplant recipients had a mean age of 28.2 ± 3.4 years. Hypertension was the most common complication in the third trimester with a rate of 46.6% in our population. Although all the pregnant kidney transplant recipients gave a successful birth and no maternal complication has been experienced in our center, all the newborns had premature birth and low birth weight and small for gestational age infants. All the newborns have been discharged after an average duration of hospital stay of 14.6 ± 4.2 days.

Conclusion: Pregnancy after kidney transplantation is a period with potential risks for mother, newborn and the allograft. Planned gestation, regulation of immunosuppressive and other drugs, close follow-up with cooperation of O&G and transplantation unit is essential and showing excellent results in pregnant kidney transplant recipients and their newborns.

P8.113

Starting a New Life Thanks to a Successful Kidney Transplant After 30 Years of Hemodialysis: Case Report

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1Department of General Surgery, Division of Transplantation, Baskent University, Ankara, Turkey; 2Department of Nephrology, Baskent University, Ankara, Turkey.

Introduction: Chronic kidney disease (CKD) has devastating effects, especially on children. Complications that develop secondary to chronic kidney disease at an early age may negatively affect the remaining period of the patient. As is known, the only curative treatment for CKD is kidney transplantation (KT). Thanks to KT in a short time after the diagnosis of CKD, the development of complications can be prevented or the complications can be recovered. In our study, we evaluated our patient who had CKD since the age of 7 and had a kidney transplant at our center after 30 years.

Methods: Our patient, who did not have any disease before, was given beta lactam antibiotic therapy for pneumonia at the age of 7 years. After the treatment, the patient developed peripheral edema and decreased urine output. In the examinations performed for these reasons, the patient was diagnosed with drug-induced nephritis and hemodialysis treatment (HD) was started. After 1.5 years of HD, a peritoneal dialysis catheter was inserted for the purpose of peritoneal dialysis. However, 20 days after the peritoneal dialysis catheter was placed, the patient underwent laparotomy due to intra-peritoneal bleeding. 4 days after the first laparotomy, the patient underwent a repeat laparotomy due to acute appendicitis and appendectomy was performed. In the following period, the patient received HD 3 times a week. In addition, the patient developed calcium deficiency and growth retardation. Skeletal deformities, dwarfism and dental deformities developed in the patient. In addition, the patient was infected with the hepatitis C virus due to blood transfusion. After the patient admitted to our center for treatment, all medical treatments of the patient were revised and he was added to the waiting list because he did not have a suitable donor. The bladder capacity was determined as 10 cc. Hydrodilatation was applied to the patient in order to expand the bladder volume. KT from a deceased donor was performed by our team on January 06, 2022.

Results: No complications were observed in the patient during the KT and in the postoperative period. On the 7th postoperative day, the patient had a urine output of approximately 5000 cc/day. Thanks to the previous hydrodilations, the bladder capacity has reached a satisfactory and comfortable level. The creatinine level of the patient decreased to 1.02 mg/dL on the 3rd postoperative day. The serum calcium level increased to 10.7 mg/dL after KT. The hemoglobin level increased from 7 g/dL to 13 g/dL.

Conclusion: Kidney transplantation is the only treatment option to return to healthy life, especially for patients diagnosed with chronic kidney disease at an early age. Thanks to early successful kidney transplants in experienced centers, patients can lead a comfortable life socially and medically.
P8.114

Recurrence Rate of Early HCV Infection After Renal Transplantation Following Successful Treatment of Dialysis Patients With Direct Acting Antiviral Agents

Farina Muhammad Hanif1, Asha Devi1, M. Danish Wallam1, Nasir Hassan Luck1, Syed Mudassir Laeeq1, Abbas Ali Tasneem1, Tahir Aziz2.

1Hepatogastroenterology, Sindh institute of Urology and Transplantation, Karachi, Pakistan; 2Transplant Science, Sindh institute of Urology and Transplantation, Karachi, Pakistan.

Introduction: HCV recurrence after organ transplantation has dreadful complications. Excellent response of direct acting antiviral agents (DAAs) in transplant recipients has been reported in various studies. Although, sustained virological response is considered as the virological cure, but it requires patients to be further 3 months on dialysis before undergoing renal transplant. Thus, increasing risk of HCV re-infection and associated complications. We aim to determine HCV recurrence in renal transplant recipients (RTRs) who has achieved end of treatment response (ETR) before transplant.

Methods and Materials: As per institutional protocol dialysis patients who failed to achieve rapid virological response (RVR) were treated with 6 months of DAAs. All patients who have achieved ETR were then referred for transplantation. Kidney transplant recipients who were treatment experience with DAAs and had a HCV PCR done 3 months after transplant was enrolled. Participant's demographic and clinical data was documented and statistical analysis was performed by SPSS 20.0.

Results: In total 40 transplant recipients were included, majority were males (81.1%) with mean age of 28.7 ± 9.4 years. All patients had received sofosbuvir, daclatasvir and ribavirin combination prior to transplant. Majority of patients received treatment for 3 months (70%). Only 5% of study population did not achieved RVR while all patients achieved ETR. Two patients also had treatment experience with interferon. Post-transplant HCV PCR was conducted at mean duration of 8.3 ± 3.3 months. Laboratory parameters showed Total Bilirubin 3.6 ± 17.5 mg/dL, Alanine transaminase 51.5 ± IU/L, and gamma glutamyl transferase of 133.9 ± 220 IU/L. Post renal transplant HCV recurrence was documented in 2 (5%) recipients.

Conclusion: This is first study to document excellent response of DAAs in renal transplant recipients who has been referred early for transplant. Thus, dialysis patients can undergo transplant after achieving end of treatment response.

P8.115

Polyomavirus Infection in the Urine for Follow-up of Renal Transplant Patient: A Single Center Study

Ho Trung Hieu1, Bui Tien Sy2, Nguyen Manh Dung3.

1Department of Nephrology, Urology, Transplantation, 108 Military Medical Hospital, Ha Noi, Viet Nam; 2Department of Microbiology, 108 Military Medical Hospital, Ha Noi, Viet Nam; 3108 Military Medical Hospital, Ha Noi, Viet Nam.

Background: Polyomavirus BK and JC are the most common viral infection after renal transplantation. The current evidence shows that both virus infection has a greater risk on kidney graft function, leading the management of viral infection is becoming a major challenge.

Methods: We included 89 patients including 70 males and 19 females (follow up of 104 patients, mean follow-up 16.66 months) who were transplanted at 108 Military Central Hospital between December 2016 and December 2021. BK and JC polyomavirus screening was performed every 3 months within the first year after kidney transplantation, and every 6 months after year-1, or when any clinical infection symptoms were recognised by the physician. Multivariable Cox-regression analysis was performed to evaluate risk factors for the onset of BK, JC infection.

Results: 317 episodes of BK and JC infections were detected in 71 patients (52.8%) included Polyomavirus BK (26.0%), JC (21.8%), and BK and JC co-infection (5.0%). The mean time until onset of BK (15.39±20.06 months) was significantly earlier than JC (21.74±19.75 months), p<0.01. Risk factors for BK infection were hypertension (p<0.05, HR 1.79), and eGFR (p<0.05, HR 1.02). For sole JC infection, Systolic blood pressure (p<0.01, HR 1.06), Mycophenolate mofetil dose (p<0.001, HR 1.003). For the occurrence of co-infection, BMI (p<0.001, HR 1.25) and HDL-C (p<0.05, HR 1.25) were revealed as the most relevant factors. Male (p<0.05, HR 0.07) and eGFR (p<0.01, HR 0.94) were identified to reduce the risk of co-infection.

Conclusion: Our results showed hypertension and eGFR were independent risk factors for BK infection, while high Systolic blood pressure and high dose of mycophenolate mofetil for JC infection. BK and JC co-infection was associated with gender, BMI, HDL-C and eGFR. The result provided initial evidence for appropriate control and the prevention of Polyomavirus infection.
Evaluation of Traditional and Non-traditional Lipid Components in Renal Transplant Recipients


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Introduction: Kidney transplantation is followed by development of additional cardiovascular risk factors. The conventional lipid markers like triglyceride, cholesterol, LDL and HDLs are generally measured as traditional lipids to identify subjects at risk of cardiovascular events. But there are other potential atherogenic risk elements like Apolipoprotein A-1, B and lipoprotein (a). When included, these may provide better assessment of dyslipemias in renal transplant recipients. In this study we evaluated the dyslipidemia status in a group of living related kidney recipients by seeing the pattern and interaction of both groups of traditional and nontraditional lipids.

Materials & Method: In this cross sectional study renal allograft recipients, at least 3-month post-transplant, were included. Laboratory investigations done were triglyceride (TG), cholesterol (TC), low density lipoprotein (LDL) and high-density lipoprotein (HDL) as traditional lipid marker and Apolipoprotein B (APO B) and A1(APO A-1); and lipoprotein(a) (lipo(a)) as non-traditional lipid markers. Tests for glycaemia (HbA1c), renal function (ACR, serum creatinine, eGFR), anemia (hemoglobin) and inflammation (hsCRP) were also done.

Results: In this study 105 patients were included. They were mostly on triple drug therapy with tacrolimus, mycophenolate mofetyl and prednisolon. The duration of transplantation was 34±26 (4.5-112) months. Mean age was 34 ± 8 years with a male to female ratio was 7:1. The mean serum creatinine was 2.0±1.3 mg% and eGFR 52± 8 years with a male to female ratio was 7:1. The mean serum creatinine was 2.0±1.3 mg% and eGFR 52±1.3 ml/min/1.73m2. Among renal transplant recipients, 62% had elevated TG (> 150mg %), 33% had elevated TC (> 200mg %), 53% had elevated LDL (> 100mg %) and 61% had low HDL (<40mg %). The ApoA-1 was below normal (<120mg % in male and < 140 mg% in female) in 43%. Apo B elevated (> 130mg %) in 10% and Lipoprotein (a) elevated (> 30mg %) in 16%. According to abnormality in any of the traditional lipid markers 88% of the renal transplant recipients was identified with dyslipidemia. According to abnormal cut-offs dyslipidemia was identified by non-traditional lipid markers in 57%. In 12% subjects all traditional lipid markers was normal but abnormal when nontraditional ones were checked. In all subjects with traditional dyslipidemias 41% had normal nontraditional lipids. In 52% subjects both traditional and nontraditional lipid markers were in dyslipidemic range.

Conclusion: Both traditional and nontraditional lipid parameters are needed to be measured in renal transplant recipients to identify the pattern and extent of dyslipidemia prevails among them. This will help in better lipid management and prescribing anti- lipid therapy to combat cardiovascular events.

A Real-World Non-interventional Research Study of Kidney Transplant Patient Characteristics, Treatments, And Outcomes in the UK

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Introduction: Despite improvements in long-term graft and patient survival in kidney transplant, there remains significant unmet need arising from the long-term exposure to immunosuppressant drug regimes. We report the outcomes in kidney transplant recipients using a retrospective, non-interventional cohort study using real world data (RWD).

Methods: All patients with end stage renal disease (ESRD; ICD-10 N18.0) or chronic kidney disease stage 5 (ICD-10 N18.5) who were recipients of a kidney transplant centre in England, were followed up until 31/12/2020. Baseline characteristics of the patients at index were retrieved from their electronic health records (EHR) and immunosuppressant therapy data retrieved from hospital pharmacy records. Graft rejection, overall survival (OS) by Kaplan-Meier, and adverse events as recorded in EHR were stratified by age, sex, ethnicity, deprivation (score 0-10; 0 being least deprived), and immunosuppressive therapy regimen.

Results: Of the 975 kidney transplant patients 63% were male, the mean age was 51.4 years (SD 13.5), 60.5% were white, and the mean deprivation score was 6.3. The most common comorbid conditions among the cohort were hypertension (32%) and diabetes 1 or 2 (20%). Tacrolimus (94%), mycophenolate mofetil (85.6%), and methylprednisolone (83%) were the top three immunosuppressant therapies prescribed by the hospital pharmacy. 1-year, 3-year and 5-year OS of 97% (CI95% 95.9-98.1), 92.3% (CI95% 90.5-94.2) and 83.7% (CI95% 80.6-87.1) respectively.

Conclusion: This study provides a real-world insight into the patient characteristics, current treatments and outcomes of patients with kidney transplant in the UK stratified by ethnicity, deprivation score, and treatment patterns. RWE studies, such as this current one, provide vital evidence to benchmark findings of future clinical trials. This data could also form the basis for AI-driven predictive patient pathway modelling based to help inform and support clinician decision making.
P8.118

Effect of Donor vs Recipient Delta of Age and BMI on Kidney Transplantation Outcome

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¹Division of General and Transplant Surgery, Azienda Ospedaliera Universitaria Pisana, Università di Pisa, Pisa, Italy; ²Division of Endocrinology, Azienda Ospedaliera Universitaria Pisana, Università di Pisa, Pisa, Italy.

Introduction: An ongoing challenge is the significant gap between organ supply and demand, which requires increased awareness for organ donation and for the decision-making process in accepting a graft. A donor offer requires careful consideration of various features, both donor and recipient, and despite the acute shortage of graft for kidney transplantation, each year more cadaveric kidneys are discarded because of unsuitability. The purpose of the study is to evaluate the effect of the difference of age and BMI between donor and recipient on single kidney transplantation (SKTx) outcome.

Method: We considered all patients underwent deceased SKTx from 2005 to 2021 at a single Center. The Δ-age was calculated as the difference between donor’s and recipient’s age. The Δ-BMI was calculated as the difference between donor’s and the recipient’s BMI. The effect of Δ-age and Δ-BMI was calculated, as odd ratio (OR), with respect to PNF, DGF, acute rejection, 3-month and 1-year eGFR. The ROC curve analysis was used to determine the cut-off value of significance of the Δ-age and Δ-BMI on the outcome.

Results: 354 SKTx were included in the analysis. The median Δ-age was 5 (range 0/11) years. The Δ-age was statistically associated to PNF (p=0.01), with an OR 1.11 (1.02-1.21), to DGF (p=0.03), with an OR 1.03 (1.00-1.05), and to acute rejection (p=0.0049), with an OR 1.05 (1.01-1.09). The Δ-age was also statistically associated to 3-month and 1-year e-GFR (p<0.001, est=-0.37 ±0.09 and p=0.004, est =-0.31 ±0.11). The cut-off value of Δ-age >19 years is associated to a higher PNF rate and lower e-GFR so could be a useful parameter to evaluate in case of fragile recipient. Δ-age can be an easy parameter for immediate help in deciding if accepting or declining a donor according to the selected recipient.

P8.119

Simultaneous Pancreas-Dual Kidney Transplantation: A Case Report

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¹Division of General and Transplant Surgery, Azienda Ospedaliera Universitaria Pisana, Università di Pisa, Pisa, Italy; ²Division of Metabolism, Azienda Ospedaliera Universitaria Pisana, Università di Pisa, Pisa, Italy; ³Division of Endocrinology, Azienda Ospedaliera Universitaria Pisana, Università di Pisa, Pisa, Italy.

Introduction: The quality of pancreas and kidney grafts from deceased donors can be extremely wide and age is not a reliable parameter of evaluation. Young donors should be carefully evaluated, in case of dubious clinical data, biopsy used to evaluate the graft and decide whether to perform a single or a double kidney transplant. We present a case involving a young donor with a kidney biopsy score unexpected in relation to her age and known comorbidities.

Method: Organs from a 43-year-old woman (BMI 31.0 Kg/m²), brain dead donor due to cerebral hemorrhage, CMV IgG positive, KDPI 46%, KDRI 0.96, PDRI 1.88 were offered for a simultaneous pancreas-kidney transplant. Donor apparently had no comorbidities but a serum creatinine of 1.50mg/dl (e-GFR 40.9ml/min) to hospitalization, worsened during the observation period. Wedge kidney biopsies (159/208 glomeruli) were performed, graded according Karpinski-Remuzzi score 8/12 for each of the two kidneys (glomerular sclerosis: 1/3, tubular atrophy: 2/3, interstitial fibrosis: 2/3, arterial narrowing: 3/3). Due to these unexpected data, it was performed a simultaneous pancreas-double kidney transplantation on a 49-year-old man (BMI 24.2 Kg/m²) with type 1 diabetes, laser treated diabetic retinopathy and end stage renal disease on dialysis (since 4 years).

Results: Transplantation was performed placing pancreas in retrocolic position with systemic-enteric drainage (vena cava and Roux-en-Y jejunal loop) and was completed placing the left kidney in the left iliac fossa and the right kidney in right iliac fossa. Cold ischemia time lasted 485 min for pancreas, 600 min for right kidney and 680 min for left kidney. Induction immunosuppression was obtained with basiliximab and steroids. Maintenance was based on LCP tacrolimus(Envarsus®; Chiesi, Italy), mycophenolic acid (720 mg twice a day) and steroids, rapidly tapered. On POD 7, recipient suffered of spontaneous pneumothorax. The following postoperative period was uneventful and he was discharged with 1.7 mg/dl serum creatinine. At 1-year follow-up he is insulin-independent and serum creatinine is 2.0 mg/dl.

Conclusion: According to Karpinski-Remuzzi’s criteria, the high biopsy score would not have allowed the single kidney transplant. It was also conflicting with the donor’s age that would not have required a biopsy based on her medical history. However, it was decided to perform a SPDKTx to improve the patient outcome rather than to perform a pancreas transplant alone leaving the patient on dialysis. The donor kidney biopsy remains a very helpful tool in the evaluation of the graft. However, it is a data to be interpreted case-by-case.
Impact of Desensitization in Immunological Low-Risk Patients in Kidney Transplantation

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Background: Pretransplant DSA is considered to increase the risks of early rejection and long-term graft failure in kidney transplantation (KT). However, there is a lack of consensus on whether desensitization before transplantation is necessary for patients with low mean fluorescence intensity (MFI) value of donor specific antibody (DSA). In ABO-incompatible (ABOi) KT, recipients underwent pretransplant desensitization treatment, using rituximab, plasmapheresis (PP), or intravenous Ig (IVIG). This study aims to examine the efficacy of pretransplant desensitization in immunological low-risk patients by comparing the incidence of one year de novo(dn) DSA in ABOi and ABO compatible (ABOc) KT.

Methods: This retrospective observational study included pre-transplant DSA positive recipients with maximal DSA MFI <5000 and negative flow-cytometric crossmatching (FCXM) between January 2014 and December 2019. A total of 274 patients were divided into an ABOc (n=222) and an ABOi (n=87) group.

Results: The baseline characteristics showed no difference between the two groups except the degrees of PRA class I and II were significantly higher in the ABOc group (P = 0.010 and P = 0.036). The incidence of dn DSA during one year after KT was significantly lower in ABOi group than in the ABOc (n=34, 15.3% vs. n=2, 3.8% P = 0.028). Multivariate analysis indicated that ABO incompatibility was the only significant factor associated with the development of one year de novo DSA (OR[CI], 0.22 [0.05 – 0.95]; P = 0.043). Overall rejection-free survival was inferior in patients who developed the dn DSA within one year than in patients without dn DSA for one year following KT (P < 0.001).

Conclusions: Pretransplant desensitization in patients with positive DSA and FCXM may have beneficial effects on the development of dn DSA. These results indicate the need for studies in larger patient cohorts, including randomized controlled trials, to examine the effectiveness of pretransplant desensitization in immunological low-risk patients in ABOc KT.

Table 1. Demographics and clinical characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>ABO compatible (N = 222)</th>
<th>ABO incompatible (N = 52)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>47.3 ± 12.7</td>
<td>30 (57.7)</td>
<td>0.949</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.8 ± 3.7</td>
<td>30 (57.7)</td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Duration of dialysis (months)</td>
<td>18.8 ± 38.9</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Donor</td>
<td></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Living donor</td>
<td>151 (68.0)</td>
<td>52 (100.0)</td>
<td></td>
</tr>
<tr>
<td>Deceased donor</td>
<td>71 (32.0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Previous transplant</td>
<td>23 (10.4)</td>
<td>3 (5.8)</td>
<td>0.570</td>
</tr>
<tr>
<td>HLA-A, -B, -DR mismatch</td>
<td>3.7 ± 1.4</td>
<td>3.9 ± 1.3</td>
<td></td>
</tr>
<tr>
<td>PRA class I</td>
<td>40.5 ± 35.6</td>
<td>27.5 ± 29.5</td>
<td>0.019</td>
</tr>
<tr>
<td>PRA class II</td>
<td>36.7 ± 33.5</td>
<td>26.1 ± 27.6</td>
<td>0.036</td>
</tr>
<tr>
<td>Class I DSA positive</td>
<td>127 (57.2)</td>
<td>31 (59.6)</td>
<td>0.752</td>
</tr>
<tr>
<td>Class II DSA positive</td>
<td>112 (50.5)</td>
<td>27 (51.9)</td>
<td>0.848</td>
</tr>
<tr>
<td>Class I DSA, MFI</td>
<td>1296 ± 1352</td>
<td>1219 ± 1261</td>
<td>0.707</td>
</tr>
<tr>
<td>Class I DSA, MFI</td>
<td>1063 ± 1332</td>
<td>1069 ± 1522</td>
<td>0.615</td>
</tr>
<tr>
<td>Both Class I and II DSA positive</td>
<td>17 (7.7)</td>
<td>6 (11.5)</td>
<td>0.364</td>
</tr>
<tr>
<td>De novo DSA within 1 year</td>
<td>34 (15.3)</td>
<td>2 (3.9)</td>
<td>0.028</td>
</tr>
</tbody>
</table>

Figure 1. Rejection free graft survival rate after transplantation
Inguinal Herniation After Kidney Transplantation


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Introduction: There have been some reports of transplant ureteral obstruction due to inguinal hernia after kidney transplantation (KT). This study aims to clarify the clinical features and the outcomes of ipsilateral inguinal hernia after kidney transplantation.

Method: From 2011 to 2020, eight patients who diagnosed as inguinal hernia on the ipsilateral side of KT were included in this study. We retrospectively reviewed those patient’s clinical data from medical records. All values were expressed as the median and range. This study was approved by the ethics committee of the Institutional Review Board.

Results: All patients were male. The age was 68 (range, 28 - 75) years. Of the eight patients, living donor KT was performed in 5 and deceased donor KT was performed in 3. The median post-transplantation period was 6.8 (0.5 - 18.0) years. Right side inguinal hernia was observed in all patients, including one case of bilateral inguinal hernia. Six patients were direct type and two were indirect type of inguinal hernia. The hernia contents were transplanted ureter and bladder in 2, transplanted kidney and ureter and small intestine in one, transplanted kidney and small intestine in one, bladder and small intestine in 3, and only bladder in one patient. Five out of 8 patients showed transplant urinary tract obstruction due to inguinal hernia. All hernias were repaired by using meshes (mesh plug method in 6, Lichtenstein method in 2). The operative time was 120 (86 - 155) minutes and blood loss was 7 (2 - 85) ml. Serum creatinine levels in five urinary obstructed patients were improved (p < 0.01) and transplanted urinary tract obstruction was disappeared after surgery. During follow-up period, no recurrence of inguinal hernia was observed and only chronic pain in the groin area (Clavien-Dindo grade II) was complicated in one patient.

Conclusion: According to the previous 23 published cases, the median age at presentation was 59 years and median post-transplantation period was 11.5 years. Right side inguinal hernia was 65%, and 91% of inguinal hernias were presented ipsilaterally to the graft. As initial treatment to avoid graft failure, percutaneous nephrostomy (61%) and ureteral stenting (39%) were frequently reported. Transplant ureteral obstruction due to inguinal hernia is a rare complication after kidney transplantation. However, transplant ureter or bladder herniation should be considered in the differential diagnosis of graft hydronephrosis for preventing allograft loss. Surgical intervention for inguinal hernia after kidney transplantation was safe and effective treatment to prevent worsening kidney graft function.

Tacrolimus Dose Reduction as an Effective Therapeutic Approach to the Patients With Active BK Virus Replication And Nephrotoxicity

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Background: BK viral nephropathy (BKVN) affects a significant proportion of kidney grafts in the early post-transplant period and often leads to functional failure of these grafts. The intensity of immunosuppressive therapy plays a significant role in the activation of BK viral (BKV) replication.

Methods: 457 per-protocol biopsies of kidney grafts were performed in a group of 161 newly transplanted patients. The incidence of histological signs of tacrolimus nephrotoxicity as a manifestation of excessive immunosuppression was calculated using the Calcineurin Inhibitor Nephrotoxicity Score (CINS). In case of detection of simultaneous toxicity and substantial BKV replication, the dose of tacrolimus and/or mycophenolate was reduced and the effect on the inhibition of BKV activation and regression of toxic changes was compared. In parallel, we studied the effect of pre-emptive reduction of tacrolimus dose on the development of BKV replication in isolated detections of toxicity during the subsequent period.

Results: The reduction of tacrolimus and mycophenolate dose in patients with histological evidence of toxicity and significant BKV replication was associated with an early and significant decrease in the BKV plasma load compared to isolated mycophenolate reduction (P = 0.023), significant decrease in CINS (P = 0.001) and better functional parameters at the end of this one-year follow-up (P = 0.024). A pre-emptive dose reduction of tacrolimus in case of toxicity evidence led to a marked reduction in the incidence of substantial BKV viremia during the subsequent period.

Conclusions: The reduction of tacrolimus and mycophenolate dose in patients with histologically verified tacrolimus nephrotoxicity represents a more effective approach to attenuate significant BKV replication than a single-dose reduction of mycophenolate, including the regression of toxic changes. Pre-emptive tacrolimus dose reduction in case of toxicity signs is associated with a lower incidence of significant BKV replication during the first year after transplantation, without increasing the risk of acute rejection. Supported by MHČZ – DRO (FNOI, 00098892) and by grant IGA_LF_2022_03.
A Retrospective Comparison of ABO Incompatible With ABO Compatible and Cadaveric Renal Transplant: Single Centre Experience

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Introduction: ABO incompatibility was a major barrier in kidney transplantation. Advances in immunosuppressive therapy and desensitization protocol have made ABO incompatible transplants safe and effective. The present study is a retrospective comparison of ABO incompatible with ABO compatible and Cadaveric renal transplant in single centre.

Method: The study includes 7 ABO incompatible, 14 similar age and HLA matched ABO compatible and 7 cadaveric kidney transplant recipients. All ABO incompatible recipients underwent desensitization with Rituximab and plasmapheresis with IVIg. Their outcomes at 6 months in terms of eGFR calculated by MDRD formula, incidence of rejection and infection as well as graft survival and patient survival were compared.

Result: The outcome in terms of eGFR at 6 months was equivalent in ABO compatible (66.90ml/min/1.73m2) and ABO incompatible (60.42ml/min/m2) group and was significantly lower in the cadaveric group (45.32ml/min/m2). The incidence of infection at 6 months was equal in ABO incompatible (28.5%) and ABO compatible group (28.5%) and it was significantly higher in cadaveric transplant groups (42.85%). There was one incidence of acute rejection and one graft loss in cadaveric transplant group whereas no rejection and graft loss in ABO compatible and ABO incompatible transplant group. All three groups had 100% patient survival.

Conclusion: The graft function, risk of infection and graft survival at 6 months in ABO incompatible transplant is non inferior to ABO compatible transplant and is superior to Cadaver transplant. ABO incompatible transplant also circumvents the waiting period on dialysis and mortality and morbidity associated with it.

Recurrence of Focal Segmental Glomerulosclerosis After Kidney Transplantation According to Pre-transplant Treatment

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Background: Focal segmental glomerulosclerosis (FSGS) recurrence after kidney transplantation (KT) is a significant risk factor of graft failure. The recurrence of FSGS develops in 30%–60% of recipients following KT. However, there are few proven clinical markers and risk factors related to FSGS recurrence. To our knowledge, there is no proven evidence for the efficacy of pretransplant conditioning in FSGS. In this study, we evaluated the recurrence rate of FSGS after KT according to pre-transplantation treatment and identified the risk factors associated with recurrence.

Methods: A total of 99 patients who underwent KT due to FSGS at the Asan Medical Center between 2007 and 2018 were included in the study. These patients were divided into the pretreatment group (N = 53) and no pretreatment group (N = 46) according to pretransplant treatment.

Results: The pretreatment group had a significantly shorter dialysis duration than the no pretreatment group (19 vs. 65 months; p < 0.001). FSGS recurrence was less frequent in the pretreatment group [5 (9.4%) vs. 16 (34.8%); p = 0.002]. All three cases of graft failure due to recurrent FSGS occurred in the no pretreatment group. FSGS recurrence after KT was significantly related to age (HR = 0.63, p = 0.014) and pretransplant treatment vs. no treatment (HR = 0.20, p = 0.004). The pretreatment group showed no difference in overall graft survival compared to the no pretreatment group (p = 0.37) but had a superior death censored graft survival (p = 0.04).

Conclusion: The study suggests that pre-transplantation treatment, such as plasmapheresis and rituximab administration, may reduce FSGS recurrence after KT. We recommend preventive plasmapheresis immediately after transplant in patients in whom applying pretransplant treatment was difficult and careful monitoring of such patients for proteinuria.
Abstracts

P8.125

Anti-thymocyte Globulin Versus Basiliximab Induction For Kidney Transplantation in Elderly Patients: Matched Analysis With Korean Multicentric Registry

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¹Nephology, Yonsei University Wonju College of Medicine, Wonju, Korea; ²Surgery, Severance Hospital, Seoul, Korea.; The Korean organ transplantation registry study group.

Introduction: Basiliximab (BSX) and anti-thymocyte globulins (ATG), are two major immunosuppressive agents commonly used as induction therapy for kidney transplant (KT) recipients. The superiority of ATG over BSX has not been well established especially in elderly KT recipients with low immunological risk.

Method: A total of 847 elderly (≥60 years) low-risk KT patients in the Korean Organ Transplantation Registry were matched with 2:1 propensity scores and compared according to the ATG and BSX induction therapy. The primary outcome was patient and graft survival. The secondary outcome was biopsy-proven rejection, graft function, BK virus nephropathy, infection, cancer, new-onset diabetes mellitus after transplantation (NODAT), and delayed graft function.

Results: 165 patients in the ATG group were matched to 298 patients in the BSX group with an average age of 64.3 and 64.2 years, respectively. During 28.5 ± 10.4 months of mean follow up the cumulative probability of death censored graft failure at 3-year posttransplantation were 1.3% and 1.4% in ATG and BSX group without significant difference (p = 0.720). Cumulative probability of NODAT at 3-year posttransplantation was significantly higher in BSX group (35.6% versus 21.6%, p = 0.021). Median Tacrolimus trough level was significantly lower in 6 months after kidney transplantation in the ATG group (5.7 ng/mL versus 6.4 ng/mL, p = 0.001). There was no difference in other evaluated outcomes.

Conclusion: Compared to BSX, in elderly low-risk KT, ATG reduced Tacrolimus and steroid requirements without all-cause mortality, rejection, infection difference. Resulting in reduced NODAT incidence.

P8.126

Angiotomography in the Vascular Assessment of Recipients Before Renal Transplantation: A Profile of Excluded Patients

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Introduction: Arterial calcification and atherosclerotic lesions, which have a high incidence in chronic renal patients, are important risk factors for immediate and late postoperative complications after renal transplantation. Computed tomography angiography of the iliac arteries can accurately show arterial diseases, including the location and extent of arterial calcification, as well as arterial caliber, which would allow better surgical planning of the site of renal implantation.

Objective: The objective of this study was to stablish the profile of patient that were removed from the waiting list as a result of extensive calcification affecting iliac vessels and to assess the value of CTA diagnostic method for verifying calcification affecting iliac vessels in candidates to renal transplantation.

Methods: It was assessed data of 121 patients in the waiting list who underwent abdominal CTA in prior transplant evaluation between February 2015 and August 2020. Inclusion criteria to be undergone to CTA were patients older than 50 years and that filled some one of the following conditions, like diabetes mellitus; hypertension and vascular events.

Results: Sixty-nine (57,02%) patients were classified “not a transplant candidate” (NATC) by absent adequate vascular free area to arterial vessels anastomosis. Fifty-two (42,97%) patients were considered adequated, keeping in the waiting list. There was not statistically significant difference between groups in mean age, dialysis duration mean and comorbidities: diabetes mellitus, hypertension and the both. Previous history of vascular events (isquemic brain stroke, cardiovascular phenomenons or peripheral vascular disease) was most frequent in the NATC group (p<0,05).

Conclusion: Apparently, previous history of cardiovascular events was the factor that better reflected vascular conditions of pelvic region. Computed tomography angiography had a significant value in detecting vascular calcifications, allowing better surgical planning.
Risk Factors for Chronic Allograft Rejection After Kidney Transplantation: A Systematic Review and Meta-Analysis

Geode Wira Mahaditta1, I Gede Raka Widiana2

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Introduction: Kidney transplantation has better outcome compared to dialysis patients. With high demand and low supply, it is important to maximize graft longevity. One of risk factors for graft failure is allograft rejection. Chronic allograft rejection occurs months or years after transplantation. Multiple studies have been analyzing risk factors for this entity. Our study aimed to evaluate risk factors for chronic allograft rejection after kidney transplantation.

Method: We systematically searched Pubmed, Directory of Open Access Journal (DOAJ), Cochrane Central Register of Controlled Trials (CENTRAL) and Science Direct on March 8th, 2022.

Result: Total ten studies of 25,774 kidney transplant patients were included in this study. Mean age difference between chronic allograft rejection and non-chronic allograft rejection was -3.41 years (p < 0.00001). Human leukocyte antigen (HLA) was a risk factor. Lower body surface area (BSA) ratio was associated with higher risk. Higher triglyceride and IL-6 was a risk factor. In association with kidney function, worse kidney function (proteinuria, higher creatinine post-transplant and higher urea) was a risk factor. Acute rejection was a risk factor (RR 2.57 [1.91, 2.96]; p < 0.00001; I2=7%; p = 0.30). Low cyclosporin A (CsA) whole blood trough levels post transplantation (< 110 ng/mL) was a risk factor.

Conclusion: Younger recipient age, HLA, lower BSA ratio were risk factors for chronic allograft rejection. Post transplantation, worse kidney function, higher triglyceride, higher IL-6, acute rejection and low CsA whole blood trough levels were risk factors.

The authors would like to thank all authors from the analyzed studies. The authors would also thank all staff of the Division of Nephrology and Hypertension in Department of Internal Medicine in Udayana University Sanglah Hospital, Denpasar, Bali-Indonesia.
**P8.129**

**Description of the Process of Inclusion and Kidney Transplantation Waiting List - Uruguay**

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**Introduction:** In Uruguay with 3,286,314 inhabitants (2011 census), renal transplantation is performed in 3 transplant centers, is regulated by the Instituto Nacional de Donación y Trasplante (INDT) and financed by the Fondo Nacional de Recursos. The allocation is made on a national algorithm and it is an INDT's responsibility. In the last 5 years, including the Health Emergency, an average of 139 kidney transplants were performed per year. The average rate for these 5 years of renal transplantation is 42.33 pmp.

**Objective:** Describe the renal waiting list (WL) admission process and the recipient population.

**Methods:** The study algorithm for admission to the WL include:
- □ ABO and Rh blood group typing.
- □ HLA typing by PCR-SSO (Luminex) for A, B, C, DRB1, DQA1 and DQB1 locus.
- □ HLA antibody screening (Luminex), class I and/or II. If positive, a specificity search is performed.
- □ Search for autoantibodies by microlymphocytotoxicity technique (MLCT).
- □ Patient's serum is preserved (serum collection).
- □ PRA (wall reactive antibodies) by MLCT, defining hyperimmunized PRA>80%.

During the period in WL the following procedures are performed:
- □ Serum collection update every 3 months or after sensitizing events. Failure to comply with this requirement excludes recipients from the allocation.
- □ HLA antibody screening and specificity analysis are performed annually and PRA every six months.

**Results:** There are currently 434 patients in the WL, including one vascular emergency. Distribution - by age: 1.8% <18 years old, 85% 18-64 years old and 13.2%>65 years old; by sex: 43.8% female, 56.2% male. Blood group distribution: 54% are 0,35% A, 8% B and 2% AB. The highest immunological risk group: 18%, who aspire to be retransplanted, 1.4% hyperimmunized. There are 26.5% with positive HLA antibody screening, see table and distribution in graphs.

**Conclusions:** A single national protocol is applied at the inclusion on the WL. In the renal WL, the adult population (18 to 65 years old), blood group 0, with a male/female ratio of 1.3 prevails. The immune risk group does not present significant changes with respect to previous evaluations. The prevalence of sensitized to both classes and hyperimmunized is maintained.

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**P8.130**

**Assessing Patient-Level Predictors of Obesity for Kidney Patients Referred for Pretransplant Evaluation**

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**Introduction:** Obesity not only negatively impacts post-transplant outcomes and eligibility for kidney transplantation (KT)1 but is also associated with negative outcomes for end stage kidney disease (ESKD) patients, generally. This study assesses the impact of social determinants of health (SDOH) on the likelihood of obesity at time of referral for evaluation for KT.

**Methods:** We examined single-center kidney patient referrals from 6/2016 to 5/2021 to assess potential differential obesity at referral controlling for relevant known SDOH factors, including: socio-economic status (SES)/poverty measured by the Area Deprivation Index (ADI; a proxy SES measure utilizing Census Block Group Data to define “Neighborhood”)2 in addition to demographic factors and preemptive status (eg, patients seeking transplant referral prior to initiating renal replacement therapy). We used logistic regression to examine obesity at referral, defined as BMI>30, aligning with reconsiderations of KT BMI thresholds.3

**Results:** A total of 6129 participants were included in the study population; 60% (n=3674) were classified as obese (BMI>30). The model showed factors predictive of obesity at referral to include: increased ADI/poverty [OR: 1.39, p<0.0001; 1.26, p = 0.008; 1.37, p<0.0001, respectively], Black race [OR:1.38, p<0.0001], and preemptive status (OR: 1.26, p<0.0001). Asian patients were less likely to be obese, [OR: 0.38, p<0.0001].

**Conclusion:** With 60% of referred kidney patients presenting as obese, opportunities to intervene on nutrition, exercise, and wellness to target BMI in this population are essential to ensure that patients below the poverty level, Black patients, and preemptive patients have nutritional guidance while improving post-transplant outcomes.

**References:**
1.doi:10.1111/ajt.16196  
2.https://www.neighborhoodatlas.medicine.wisc.edu/  
Kidney Removal From the Living Donor—Technique And Evaluation: Study on 256 Samples

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Introduction: Living donor nephrectomy exposes the surgeon to a particular challenge since it involves performing a major operation on an individual who is not ill. This living donor surgery has undergone many developments. The open technique, considered the technique of choice for many years, can be performed by lumbotomy or subcostally. These two approaches are very safe in terms of mortality and morbidity. This open-air technique was used by our team to take kidney samples from all living donors. The objective is to provide an update on the technical aspects of living kidney donor surgery as well as their follow-up.

Method: From 2010 to 2020, 256 kidney samples were taken by our team (231 left, 25 right) by conventional means. The approach was the classic Lombotomy in extra-peritoneal 98% and 2% sub-costal right, 47% were men and 53% women. The average age is 46 years old (20 – 72). The donation was intra-sibling in the majority of cases: 23.5% brother, 23% sisters, 35% mother, 13.5% father, son 2.3%, daughter 1.2%, uncle 0.4%, spouse 1.5%. Preoperative CT angiography showed 1 superior polar artery in 12 cases, 2 renal veins in 9 cases and ureteral duplicity in 1 case. After complete dissection of the kidney and ureter, the adrenal and genital veins are tied, the renal artery and vein sectioned on vascular clamps and sutured. The kidney is extracted then perfused with a cold solution before conditioning and then grafted simultaneously. The main objective to minimize the risks for the donors and to obtain the best possible quality graft and to ensure the harmlessness of this act, a follow-up result of 10 years is reported.

Results: The 256 kidney samples were performed by the exclusive classical route without complication. Blood loss was less than 120ml. Operative time was on average 122 min (90-155). Warm ischemia during sampling was on average 63 sec (52-74). Cold ischemia was on average 22 min. The mean length of hospitalization was 5.7 days (4-7). Physical activity was resumed after 8 days and professional after 5 weeks. The perioperative complications are: 03 surgical revisions for hemorrhage, 03 wound sepsis and 01 parametral hematoma. Postoperative complications are: residual pain 6.25% keloid scar 2.7% hypertension 1.5%, minimal IR 0.7% evetration 2.7%, with 0% mortality.

Conclusion: We can conclude that the transplant from the living related donor finds all its legitimacy taking into account the very low risks for the donor both from the point of zero mortality in our series and from the low morbidity. Our study has also demonstrated after sufficient hindsight, lumbotomy remains for us the safest and above all the fastest way to extract a quality kidney from the donor, and which has always been entrusted to very experienced surgeons, but we must not oppose a systematic refusal to minimally invasive methods (coelio-surgery and use of the robot) which have the merit of limiting the risk of evetration and painful sequelae.

Living Kidney-Donation: Is the Donator Sheltered From Cardiovascular Risk Factors?

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Introduction: Living kidney transplantation represents the best therapeutic option for end-stage kidney disease patients. However, a multitude of questions has arisen regarding the risks encountered by the donor following kidney donation, namely cardiovascular risk factors such as diabetes and hypertension.

Methods: Herein is a monocentric, retrospective, descriptive and analytical study reporting data relative to blood pressure and glycemic equilibrium among 40 living kidney-donors that were admitted in our department of nephrology, and kidney transplantation with the purpose of donating and were followed-up in our consultation. Clinical and biological data were collected before the donation and during every visit thereafter.

Results: Median follow-up was 9 years. The median age was 42 years.75% were male.62% were married.80% of donors were related to the recipient. One donor had a history of hypertension well-controlled on monotherapy. Pre donation work up showed: the median systolic and diastolic blood pressures at baseline were 112,5 and 70 mmHg respectively and that of glycemia was 4,88mmol/l. The median time of hospitalization was 5 days. During follow-up, and comparatively, with pre-donation assessment, systolic and diastolic blood pressures were relatively stable with significantly higher blood pressure at long term only (p=0,03 for each). Two patients developed hypertension after donation and both were well-controlled on monotherapy. The median of glycemia has shown a progressive increase during the study period of 5 years with a significant difference at short and long term only (p-value of 0,02 and 0,006 respectively). One donor has developed diabetes that was well-controlled on metformin. One female donor had 2 pregnancies without gestational diabetes no hypertension or preeclampsia. No death was observed and no cardiovascular events were encountered.

Conclusion: Our results show that living kidney donation can be safely performed provided that a meticulous evaluation of the donors is ensured prior to nephrectomy. Moreover, a regular follow-up is paramount allowing an early screening for complications and a prompt initiation of treatment.
P8.133

**Metabolic Outcomes Still Occur, but Kidney Donation Is Obviously Safe**

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**Introduction:** Living kidney donation is the treatment of choice for end-stage kidney disease as it offers numerous advantages for the recipient. However, many questions regarding the prognosis of the living donor and namely the risk for metabolic complications have arisen and many studies provided reassuring results.

**Methods:** This is a retrospective, mono-centric, descriptive and analytical study reporting metabolic outcomes among 40 living donors who were admitted to our kidney transplantation center. The donors were followed-up in our consultation after discharge. During each visit, clinical and biological data were recorded and evaluated.

**Results:** Median follow-up was 9 years. The median age was 42 years. 75% were female. 62% were married. 80% of donors were related to the recipient. One donor had a history of hypertension well-controlled on monotherapy. Pre donation work-up showed that the Median Body mass index (BMI) prior to donation was 23.22 kg/m2. Four donors had obesity and seven others had overweight. The median of cholesterol and triglyceride were 4.53 and 0.91 mmol/l respectively and that of uric acid was 231 umol/l. The median time of hospitalization was 5 days. During follow-up, and comparatively, with pre-donation assessment, we noted a slight increase in the median of BMI at short and mid-terms that did not reach significance (p>0.05). We observed a significant increase in triglyceride levels at mid and long-term follow-up reaching 1.13 and 0.93 mmol/l respectively (p<0.05). The cholesterol curve after donation described an oscillating aspect with a significant difference only at mid-term reaching 4.83 mmol/l (p=0.03). Seven donors developed dyslipidemia requiring treatment with statins. Uric acid levels increased significantly from baseline at one year and stabilized at that threshold thereafter (p<0.05). Hyperuricemia was observed in six patients of whom one patient developed gout.

**Conclusion:** Our results show that kidney donation is safe provided that a meticulous screening is performed prior to donation. Metabolic outcomes could occur after kidney donation, thus regular follow-up and prompt management would help to prevent harm.

P8.134

**Advanced Cancers Treated With PD-L1 Inhibitors and CTLA-4 Antagonist in Transplanted Immunosuppressed Patients: Systematic Review of Graft Outcome**

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**Background:** Cancer is a major cause of morbidity and mortality in transplanted patients: its overall risk is increased two to three times compared to the general population, and it’s inversely related to age, with younger recipients experiencing a greater relative increase in risk compared to older recipients. Plus, the prognosis is worse for recipients diagnosed with cancer, compared to the general population, because of immunosuppressive drugs. The aim of this study is to demonstrate a correlation between use of CTLA-4 antagonist and PD-L1 inhibitors in transplanted patients with de novo malignancies and grafts outcome.

**Methods:** A literature review concerning the use of anti PD-L1 and CTLA-4 antagonists in transplanted patients with advanced neoplasms was performed. The analyzed variables were: age, sex, transplanted solid organ, immunosuppressive induction and maintenance therapy performed, type of cancer developed, development of malignancy, anticancer drugs administered, possible rejection and related therapy administered, patient outcome.

**Results:** A sample of 52 patients was sort from the literature review. The statistical analysis revealed that no variables had a significant correlation with graft rejection after the use of checkpoint inhibitors. The use of CTLA-4 antagonists seems to be associated with a less significant risk of development of graft rejection than PD-L1 inhibitors (OR = 4.00, p = 0.06).

**Conclusions:** The available data suggest that CTLA-4 antagonists are safer in transplanted patients than PD-L1 inhibitors, which were associated with a higher risk of allograft rejection. This study didn’t identify an agent responsible for differential outcomes between patients treated with PD-L1 inhibitors and CTLA-4 antagonists. Checkpoint inhibitors have proved to be valid for treatment of various malignancies, but transplanted cancer patients have never been included in clinical trials on their efficacy, because of the risk of graft rejection. Further studies and trials are needed to ensure these patients the best possible treatments.
P8.135

Machine Learning in Kidney Transplantation: A New Possibility For the Graft Survival Prediction

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Background: One of the major open questions in the field of kidney transplantation is the graft survival, and therefore life expectancy of the receiver. In the last decades the information available about the recipient, the donor and the organ transplanted have increased considerably. In addition, the knowledge about transplantation has grown, so it could be possible to make a more accurate prediction about the outcome. In the current state of the art, these analyzes are conducted by applying traditional machine learning techniques. However, these algorithms require a large and precise amount of data. Our aim is to create a new machine learning technique to predict our patients’ life expectancy and organ durability without requiring complete information and huge amounts of data to be able to produce reliable results.

Methods: To create the first algorithm, we selected only the data that by their nature could allow to compare the patients who received the kidney transplant, such as the pre and post operative creatinine value, the years of dialysis, the Charlson score etc., relating them to the age and Charlson score of the donors.

Results: Our study cohort consists of 362 patients, who underwent kidney transplantation in Ospedale di Circolo, Varese, from 2013 to 2021. Due to the incomplete nature of the data, in order to trace a patient’s life expectancy, the distance between two patients at a time is calculated considering only those features where in both patients the value is not null, otherwise the feature is eliminated for that comparison. Based on this value the distance is then calculated to find the 10 most similar patients. Finally, a post-transplant kidney longevity is calculated. A keynote from this work concerns the predictive limit of years of post-transplant organ survival. Specifically, the maximum number of years we can currently predict is 9 years given that the data we are working on have a limited range. Data processing is still ongoing, due to the limited number of the statistical sample.

Conclusions: From the preliminary results obtained, the method proposed in our study shows the potential of a system capable of obtaining an approximate but adequate estimate of the longevity of the transplanted organ. It can also be considered a starting point for the application of advanced deep learning techniques for the prediction of patients life expectancy and organ durability, which could integrate other scores already validated. Further studies are needed to improve the algorithm.

P8.136

Treatment of Calcifying Uremic Arteriopathy in a Renal Transplant Service

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Introduction: Calciphylaxis or Calcifying Uremic Arteriopathy (CUA) is a rare vascular disorder with a high rate of morbidity and mortality, of uncertain pathogenesis and with various risk factors involved. The diagnosis is suspected based on the findings in the clinical charts and physical examination, with a multidisciplinary approach. Intravenous Sodium Thiosulfate is a therapeutic alternative. Topical preparations based on cold cream from 10 to 25% could be considered as a treatment option in patients with contraindications/high risk of adverse effects for intravenous administration.

Objectives: To report the usefulness and efficacy of topical Sodium Thiosulfate treatment in patients with CUA.

Materials and Methods: We performed 938 kidney transplants between 1996 and 2022, and we assisted two patients with biopsy-proven CUA, and they received treatment with topical Sodium Thiosulfate. They presented a history of chronic kidney disease, hemodialysis, secondary hyperparathyroidism, treatment with vitamin D, diabetes mellitus, frequent traumatisms in the affected area, female sex and white race, all of them known risk factors. The affected area was:

Patient 1: ulcerated lesion on left leg.
Patient 2: multiple ulcerated lesions in both lower limbs.

Results: Skin lesions resolved completely with a preparation of topical Sodium Thiosulfate based on 25% cold cream.

Conclusions: Treatment with topical preparations of Sodium Thiosulfate based on 25% cold cream was an effective therapeutic approach in both patients with contraindications/high risk of adverse effects for intravenous administration. To the best of our knowledge, only 1 case has been reported in the literature so our experience is valuable.
P8.137
Bladder Evaluation in Transplant Patients: Are We Overdoing It?
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Introduction: It is a common practice to perform detailed bladder evaluation (DBE) in patients awaiting transplant surgery, with previous research by some noted authors Yang(1994), Peter(2004), Antoniewicz(2015) supporting this. ESRD patients on maintenance haemodialysis for more than a year eventually become anuric. For their bladder evaluation, it becomes imperative to catheterize and fill the bladder retrogradely. Catheterization thus may need to be done as high as three times, for ultrasonography (USG), micturating cystourethrogram (MCU) and uroflowmetry (UFR). This leads to bacterial colonization in bladder and results in colonization of the lower tract and a nidus for repeated reinfection. Aim of our study is thus to find out the necessity for detailed bladder evaluation in all patients & how low-capacity poor flow bladders fare post-operatively.

Methods: We studied 80 patients retrospectively for detailed reports on bladder evaluation and their follow up till one year post transplant.

Results: A very high incidence of pyelonephritis (70%) in our post- transplant patients who has undergone DBE. Additionally, some patients are still advised bladder cycling. 85% (68) of patients even with no prior history of lower urinary tract dysfunction (LUTD) or Genitourinary Tuberculosis(GUTB) had a small capacity bladder on USG and/or poor flow pre-operatively. However, in majority (90%) of them, bladder capacity and urine flow normalized as soon as urine production starts. Only a few (7 out of 68) having healthy but low capacity bladder with poor flow required some form of intervention. Patients who have healthy bladders prior to progressing to ESRD and becoming anuric fare well in post-transplant period as soon as urine production starts even if they are found to have small capacity, low flow in pre-transplant period. DBE in such patients can not only lead to overtreatment, waste resources but also increases infectious complications. Thus, we can omit MCU & UFR in pre-transplant evaluation. Only baseline USG to measure bladder capacity and thickness is all that is required. Detailed evaluation reserved only for patients having past-history of LUTD, GUTB, or bladder dysfunction like posterior urethral valves. Thus, by carefully selecting the patient, we minimized the post-transplant pyelonephritis infectious complications to 29%.

Dr. Tukaram Jamale, Professor and Head, Department of Nephrology, Seth GSVMC & KEMH All Urology and Nephrology Residents.

P8.138
Kidney Graft Survival in Pediatric Patients at the UMEA Pediatric Hospital of CMNO
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Introduction: Kidney transplantation is the gold standard for renal replacement therapy in pediatric patients with end-stage renal disease. Jalisco is the state in first place at the national level for kidney transplants, and in pediatrics it’s the UMAE Pediatric Hospital of CMNO. Renal graft and recipient survival and patient quality of life are better after kidney transplantation.

Methods: Analytical cross-sectional study with the objective of determining the survival of the renal graft in pediatric patients of the headquarters; data were collected from pediatric kidney transplant recipients performed from 2007 to 2020 at our hospital (n=715), who met the study criteria: current age under 18 years, current social security, and continued follow-up with us (n=151). A mixed model analysis was used to indicate the possible factors on the survival time of the renal graft.

Results: The average age of the recipient was 10.6 years (58.3% being male) and the donor 30.5 years (49.7% males predominated), both groups it’s more frequent O positive blood. The source of donation of the grafts (n=151) were living donors (78.1%) and cadaveric donors (21.9%). In total, 40 patients had underlying urological disease (vesicoureteral reflux most frequent), cataloging it as the main cause, however, it was striking that the undetermined had the highest percentage 38.5%, followed by hereditary 15.2%, glomerulopathies 8.6%, cystic diseases 6.6%, systemic 2.6% and HUS 1.3%. During the 13 years, 15.2% had loss, the first cause being poor adherence to treatment. The overall survival of the recipient was 97.3% and of the renal graft 84.7%.

Conclusions: The survival of the recipient and the kidney graft at our site are excellent, both comparable to those reported in developed countries. We show that the survival of living donation sources is higher than cadaveric, which is within what is expected according to international bibliography. The determined etiologies of CKD in our children were: Uropathies, hereditary, glomerulopathies, cystic, systemic and HUS. Intervening on pediatric risk factors is one of the actions implemented in our hospital to optimize the pediatric kidney transplant program.

Key words: Graft survival, kidney transplant, pediatric, factors, donor, recipient.
Progression of Chronic Kidney Disease in Pediatric Patient With Kidney Transplantation

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Introduction: The Glomerular Filtration Rate (GFR) at 1st year post transplantation is reported as a good predictor of long-term renal allograft survival after a primary kidney transplant.

Objectives: To evaluate the stage of CKD according to GFR in the first five years after transplantation in patients who received their first kidney transplant. To estimate GFR at the 1st and 5th year post transplantation and to compare them between living related donor (LRD) and deceased donor (DD) kidney transplant recipients.

Methodology: We retrospectively analyzed GFR in all pediatric primary kidney transplant recipients from January 2000 to December 2020 in our Pediatric Kidney transplant Unit at 1st and 5th year post transplantation. GFR was assessed by use of the bedside Schwartz formula.

Results: 133 pediatric c kidney transplant recipients (mean age 10.9 ± 6 yr; mean follow-up 10.23 ± 3.8 yr) were enrolled. 62% were men, in 77 (57.8%) the cause of ESKD was CAKUT; 94 (70.6%) received a LRD graft and 26 (19.5%) received a preemptive transplant. GFR and stage of CKD in the first five years after transplantation are shown in Table 1. The average drop in GFR during the first 5 years after transplant was 2.96 ml/min per year. Kaplan–Meier analysis (Figure 1) disclosed that long-term graft survival was significantly better after a LRD than DD kidney transplant (p<0.0001). But those DD kidney recipients that don’t develop graft loss had significantly higher GFR after the fifth year post transplant than LRD recipients (78.4+/−34.7 vs 61.4+/−19.4) (p<0.005). GFR was significantly decreased in those children who received a kidney graft when they were >10 years old at 5 th year (74.7+/−23.3 vs 58.1+/−26.2) (p<0.0004) after transplantation and there was no statistically significant difference in GFR in terms of the underlying CKD disease or preemptive transplantation.

Conclusion: Graft survival was significantly better after a living related donor (LRD) than deceased donor (DD) kidney transplant, but in terms of GFR, those DD kidney recipients that don’t develop graft loss had significantly higher GFR after fifth year post transplant than LRD recipients.
P8.140
Pregnancy Outcomes After Renal Transplantation. Two-Year Follow-up
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Introduction: Kidney transplant (KT) is the most effective therapeutic for women with CKD desiring pregnancy, since it allows the recovery of renal function (RF), as well as the reestablishment of the hypothalamus-pituitary-gonadal axis, ovulation and the possibility of conception. The ideal condition to get pregnant for a woman with a KT is to have stable RF, without proteinuria and controlled blood pressure. Pregnancy after KT is possible, but it is associated with a high rate of complications which are related with decreased RF, proteinuria and hypertension during and/or after pregnancy and moreover it should be taken into account the effect of immunosuppressives in pregnancy.

Objective: To describe the graft and pregnancy outcomes among KT and kidney/pancreas transplant recipients.

Material and methods: We reviewed medical records from all pregnancies that occurred in kidney and kidney/pancreas transplant women between 1990 and 2020 in 3 transplant centers in Argentina.

Results: Twenty-five pregnancies in 22 KT recipients were identified. Median age at pregnancy was 32 years and median transplant–pregnancy interval was 5 years (range,1.5-12.7 years). Forty-eight percent of the patients had hypertension, 23% had proteinuria and 8% had creatinine > 1.5 mg/dl pre-pregnancy. The most common maintenance immunosuppression was tacrolimus or azathioprine + cyclosporine + steroids (80%). Median gestational age at delivery was 37 weeks (range, 23-39 weeks). Live birth occurred in 95% of cases. There were 2 abortions. Preterm delivery rate was 40%. Forty-seven percent of newborns had low birth weight. 36% of the women had preeclampsia, 17% cholestasis and only 1 patient had gestational diabetes. At week 20 of gestation, 36% had proteinuria and 3 months postpartum the rate increased to 80%. Thirteen percent had postpartum rejection. There was a significant increase in creatinine at baseline, at week 20 and postpartum (1.12 vs. 1.15 vs. 2.18, p<0.001). Fourteen (14%) percent had lost graft function (LGF) at 2 years postpartum.

Conclusions: In this small sample, the rate of complications was high, with only 14% of LGF. We recommend the development of a nationwide registry in order to provide the true risk of maternal and fetal complications in KT in our country.

P8.141
Prevalence and Outcome of Kidney Transplant Recipients Infected With BK Polyoma Virus at National Kidney And Transplant Institute From 2016 to 2021
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Background: BK polyoma virus (BKV) infection is an evolving challenge in kidney transplant recipients as untreated infections often lead to allograft dysfunction or graft loss. The virus is ubiquitous with viremia and viruria being detected in 30% and >10% of patients, respectively. Decreasing the immunosuppression has been established as the mainstay of treatment, however, screening protocols vary between institutions.

Objective: This study aims to describe the prevalence and outcomes of kidney transplant recipients with BKV at the National Kidney and Transplant Institute (NKTI) for the last 5 years.

Methods: This is a retrospective study conducted at the NKTI where chart review was performed. Age, gender, native kidney disease, viral loads (urine and blood), graft biopsy results were reviewed. Clinical outcomes such as graft failure, early complications, and readmission were also determined.

Results: There were 1057 kidney transplants and 12 BKV cases from 2016-2021 with a prevalence of 1.1%. The mean age of recipients was 39 (range 17-66) years, majority of which were males (58%) (Table 1). Half of the recipients had chronic glomerulonephritis with anti-thymocyte globulin being the most common induction agent (67%). Majority (88%) did not have urinary stents. Of the identified cases, viremia (41%) and viruria (33%) were present with 50% having biopsy-proven BKV nephropathy. Most cases presented >6 months from transplant (66%) and viral loads were above 500 copies/ml in 83% of cases. One patient was highly sensitized (8%) and two patients had graft loss (17%). No graft loss and retransplants were done for BKV.

Conclusion: The low prevalence of BKV infection in our center reflects the varying practice of clinicians in the management of transplant recipients. Reduction of immunosuppression remains to be the treatment of choice. Early detection may prevent morbidity and graft loss. Routine screening for BKV has been recommended however, it has yet to gain acceptance among our transplant physicians.

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<tr>
<th>Age range (mean), years</th>
<th>17-66 (39)</th>
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<tr>
<td>Gender, n (%)</td>
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<tr>
<td>Male</td>
<td>7 (58%)</td>
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<tr>
<td>Female</td>
<td>5 (42%)</td>
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<tr>
<td>Native Kidney Disease, n (%)</td>
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<tr>
<td>Chronic Glomerulonephritis</td>
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<tr>
<td>Diabetic Nephropathy</td>
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<td>Gouty Nephropathy</td>
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<td>IGA Nephropathy</td>
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<tr>
<td>Hypertensive Nephrosclerosis</td>
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<tr>
<td>Induction, n (%)</td>
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<tr>
<td>rATG</td>
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<td>Basiliximab</td>
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<td>Urinary Stent, n (%)</td>
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<tr>
<td>Yes</td>
<td>2 (17%)</td>
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<tr>
<td>No</td>
<td>10 (83%)</td>
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<tr>
<td>Time to BKV diagnosis</td>
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<td>&lt;6 months</td>
<td>4 (33%)</td>
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<td>&gt;6 months</td>
<td>8 (67%)</td>
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<td>Viral Load (blood)</td>
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<td>&lt; 500 copies/ml</td>
<td>2 (17%)</td>
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P8.142

Perturbations in Podocyte Transcriptome and Biological Pathways Induced by Injury Caused by FSGS Associated Circulating Factors

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Focal segmental glomerulosclerosis (FSGS) is a glomerular histopathological lesion of some but not all glomeruli. FSGS is frequently associated with heavy proteinuria and progressive renal failure requiring dialysis or kidney transplantation. However, primary FSGS also has 40-80% risk of recurrence of disease in the transplanted kidney (rFSGS). Sera from patients with primary FSGS causes podocyte injury in culture but the injury is heterogeneous. Multiple circulating factors have been proposed to contribute to the pathogenesis of primary and rFSGS. However, neither the factors nor the downstream effectors specific to individual factors have been identified. The TNF pathway activation by one or more circulating factors present in the sera of patients with FSGS has been supported by multiple studies. Several studies have suggested a causative role for soluble urokinase-type plasminogen activator receptor (suPAR) and CD40 autoantibody in the development and recurrence of FSGS. Anti uPAR antibodies have been shown to block suPAR induced renal injury in mouse models of FSGS and commercially available anti CD40 antibodies block the development of proteinuria in mice injected with suPAR and CD40 autoantibodies purified from rFSGS patients (CD40Ab). Here we show that the podocyte injury caused by sera from FSGS patients is at least in part mediated by CD40 and suPAR by blocking the podocyte actin depolarization with a novel anti uPAR antibody (2G10) as well as a humanized commercial CD40 antibody (BMS). Additionally, we compare the molecules and pathways activated in response to CD40Ab from rFSGS patients and suPAR to that of TNFα and delineate the unique pathways associated with FSGS injury.

P8.143

Assessment of Renal Allograft Function via Urine-Based Estimation of Glomerular Filtration Rate

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Introduction: The estimation of glomerular filtration (eGFR) remains one of the most important indicators of kidney allograft health post-transplantation. eGFR has been shown to strongly correlate with graft function, and overall graft survival. Evaluation of eGFR early post-transplantation is especially crucial for understanding how well the new allograft is functioning; however, serial monitoring remains a challenge due to the requirement of frequent blood draws, and lab-based visits. We have developed a urine-based eGFR score (ueGFR) in native kidney injury patients, which has a greater than 90% correlation with eGFR formulae and classifies and predicts CKD stages with a 95% accuracy. This multi-center, longitudinal study presents the novel ueGFR score, which relies solely on urinary markers, in the context of kidney transplantation.

Methods: The previously developed ueGFR score, in native kidney injury patients, was applied to 59 unique kidney transplant patients, and 14 healthy controls. Of the 73 patients, 38% (28/73) had biopsy confirmed acute rejection (AR), and the rest had either biopsy-confirmed no-rejection (NR), or another non-rejection related post-transplant complication (ATN, FSGS, or CAN). Spearman correlation analysis was performed between ueGFR score and eGFR.non-parametric Mann-Whitney-U with Holm-Bonferroni correction for multiple comparison tests were conducted to determine differences in ueGFR and eGFR values between different phenotypes, and Kruskal-Wallis with Dunn’s post-hoc multiple correction statistical tests were conducted to determine global statistical differences in ueGFR and eGFR.ueGFR score, when applied to the 73 patients, had a statistically significant correlation with eGFR (p-value = 2.28e-13, r2 = 0.80). Furthermore, non-parametric Mann-Whitney-U with Holm-Bonferroni correction for multiple comparison tests, and Kruskal-Wallis with Dunn’s post-hoc multiple correction statistical tests showed statistically significant differences in ueGFR scores by phenotype. Kruskal-Wallis results revealed a global statistically significant difference between phenotypes (p-value = 4.7e-06), and Mann-Whitney-U with Holm-Bonferroni correction for multiple comparison tests revealed a statistically significant difference between healthy controls and acute rejection (p-value = 2.81e-06), and no-rejection and acute rejection (p-value = 0.002).

Results: Non-parametric spearman correlation results showed that the ueGFR score, when applied to the 73 patients, had a statistically significant correlation with eGFR (p-value = 2.28e-13, r2 = 0.80). Furthermore, non-parametric Mann-Whitney-U with Holm-Bonferroni correction for multiple comparison tests, and Kruskal-Wallis with Dunn’s post-hoc multiple correction statistical tests showed statistically significant differences in ueGFR scores by phenotype. Kruskal-Wallis results revealed a global statistically significant difference between phenotypes (p-value = 4.7e-06), and Mann-Whitney-U with Holm-Bonferroni correction for multiple comparison tests revealed a statistically significant difference between healthy controls and acute rejection (p-value = 2.81e-06), and no-rejection and acute rejection (p-value = 0.002).

Conclusions: The positive economic impact of early kidney function detection and its subsequent treatment cannot be underscored, enough. The inclusion of a sensitive non-invasive assay for renal function, to replace invasive eGFR tests early post-transplantation, would result in major socio-economic benefits for these at-risk populations by increasing access to easier and more frequent, low-cost and convenient GFR assessments.
Abstracts

P8.144

Regulatory T Cell Populations May Be Associated With Transplant Outcomes

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Objectives: The development of immunosuppressants has enabled remarkable progress in kidney transplantation (KT). However, current immunosuppressants cannot achieve induction of immune tolerance and their nonspecific immunosuppressive effects result in many adverse effects. Regulatory T cells (Tregs) play crucial roles in controlling allospecific immune responses. This study evaluated the distribution of Tregs and their effects on kidney allograft function in Korean KT recipients.

Methods: We enrolled 113 KT recipients with stable graft function between 1995 and 2018. Differentiation and expansion of Tregs were studied by flowcytometry to compare the Tregs subpopulations. Tregs were defined as CD4+CD25highCD127low/-FoxP3+ cells.

Results: Among the 113 patients, 73 patients (64.6%) were males and mean follow-up period was 147.5 ± 111.3 months. All patients received calcineurin inhibitors as maintenance immunosuppressants. Patients with follow-up period more than 144.3 months tended to have more gating Tregs numbers than that in shorter follow-up period (92.3 ± 142.4 vs. 50.1 ± 76.4, p= 0.061, respectively). There were no significant differences in Tregs subpopulations between patients with serum creatinine more than 1.5 mg/dL and patients with serum creatinine less than 1.5 mg/dL. In terms of the number of Tregs, when the trough level of tacrolimus was at an appropriate level, the number of Tregs tended to be higher than that of Tregs when the trough level of tacrolimus was low or high, and the organ function of the transplant was also stable.

Conclusions: Tregs counts may be associated with transplant outcomes considering that there is a relationship between these cells and kidney graft function.

Table 1. Baseline characteristics of the patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>All patients (n=113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.9 ± 9.7</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>73 (64.6)</td>
</tr>
<tr>
<td>Follow-up duration (months)</td>
<td>147.5 ± 111.3</td>
</tr>
<tr>
<td>ECDT</td>
<td>23 (21.3)</td>
</tr>
<tr>
<td>Maintenance therapy</td>
<td>110 (100)</td>
</tr>
<tr>
<td>CNI</td>
<td>109 (96.5)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>70 (61.5)</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>39 (34.5)</td>
</tr>
<tr>
<td>Sirolimus</td>
<td>73 (64.6)</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>79 (69.9)</td>
</tr>
<tr>
<td>CNIs + MMF + PDEN</td>
<td>65 (57.1)</td>
</tr>
<tr>
<td>Tacrolimus + MMF + PDEN</td>
<td>49 (43.6)</td>
</tr>
<tr>
<td>Cyclosporine + MMF + PDEN</td>
<td>9 (8.5)</td>
</tr>
<tr>
<td>Regimen</td>
<td></td>
</tr>
<tr>
<td>Tacrolimus trough level (mg)</td>
<td>5.8 ± 2.2</td>
</tr>
<tr>
<td>Cyclosporine trough level (mg)</td>
<td>9.6 ± 4.1</td>
</tr>
<tr>
<td>Pre- transplant</td>
<td>26 ± 12</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>106 ± 40</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>132 ± 7.1</td>
</tr>
<tr>
<td>Urea Creatinine (mg/dL)</td>
<td>177.2 ± 42.1</td>
</tr>
<tr>
<td>Low density lipoprotein (mg/dL)</td>
<td>100.9 ± 30.4</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>125 ± 5.2</td>
</tr>
</tbody>
</table>

Table 2. Regulatory T cell subpopulation according to the patient’s characteristics.

<table>
<thead>
<tr>
<th>Subpopulation</th>
<th>Low tacrolimus (n=57)</th>
<th>High tacrolimus (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4+CD25highCD127low/-FoxP3+</td>
<td>63.0 ± 14.2</td>
<td>75.6 ± 21.9</td>
</tr>
<tr>
<td>CD4+CD25+-CD127low/-FoxP3+</td>
<td>12.4 ± 19.2</td>
<td>12.4 ± 19.2</td>
</tr>
<tr>
<td>CD4+CD25+-CD127low/-FoxP3+</td>
<td>12.4 ± 19.2</td>
<td>12.4 ± 19.2</td>
</tr>
<tr>
<td>CD4+CD25+CD127low/-FoxP3+</td>
<td>12.4 ± 19.2</td>
<td>12.4 ± 19.2</td>
</tr>
<tr>
<td>CD4+CD25+CD127low/-FoxP3+</td>
<td>12.4 ± 19.2</td>
<td>12.4 ± 19.2</td>
</tr>
<tr>
<td>CD4+CD25+CD127low/-FoxP3+</td>
<td>12.4 ± 19.2</td>
<td>12.4 ± 19.2</td>
</tr>
<tr>
<td>CD4+CD25+CD127low/-FoxP3+</td>
<td>12.4 ± 19.2</td>
<td>12.4 ± 19.2</td>
</tr>
</tbody>
</table>
Transplantation, Guy's and St Thomas' NHS Foundation Trust, London, holistic evidenced based care. Data, will enable clinicians to identify and support at risk patients, delivering understanding the causes, and links with routinely collected biochemical experience moderate to severe depression and anxiety. Prospective study from depression or anxiety post-operatively, however, a significant proportion Most patients undergoing renal transplantation do not suffer Discussion: p<0.001), but remained within the 'minimal anxiety' range. Score at last assessment was worse than at first assessment (2.9 vs 1.9, 83.1% of patients scored minimal anxiety, followed by 9.6% reporting mild score at last assessment was worse than at first assessment (4.0 vs 2.6, 11.3% falling into moderate to severe categories. Mean annual questionnaires per patient was 3 (range 1-8). The majority of patients completing PHQ-9 and GAD-7 questionnaires, each consecutive time period. After excluding incomplete records, 599 patients were included in the final analysis. There was a male preponderance (81.0%), and median age of 54 (range 19-84). The median number of consecutive completed annual questionnaires per patient was 3 (range 1-8). The majority of patients (70.1%) scored no depression on PHQ-9, followed by 18.5% reporting mild depression, with 11.3% falling into moderate to severe categories. Mean score at last assessment was worse than at first assessment (4.0 vs 2.6, p<0.001), but remained within the 'no depression' category. With GAD-7, 83.1% of patients scored minimal anxiety, followed by 9.6% reporting mild anxiety, with the remaining 7.1% scoring moderate or severe anxiety. Mean score at last assessment was worse than at first assessment (2.9 vs 1.9, p<0.001), but remained within the 'minimal anxiety' range. Discussion: Most patients undergoing renal transplantation do not suffer from depression or anxiety post-operatively, however, a significant proportion experience moderate to severe depression and anxiety. Prospective studies understanding the causes, and links with routinely collected biochemical data, will enable clinicians to identify and support at risk patients, delivering holistic evidenced based care.

Early and Late-Onset Cytomegalovirus Infection Following Universal Prophylaxis in Kidney Transplant Recipients: Risk Factors and Outcome
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Introduction: Cytomegalovirus (CMV) is the most important viral infection in organ recipients and can be a major cause of morbidity and mortality. Most transplant centers use prophylactic therapy in patients considered to be of high risk for CMV infection (D+/R-) for 3 to 6 months after transplant. Our study aims to determine factors associated with early (defined as a diagnosis within 3 months of transplant) and delayed-onset CMV disease and association of CMV with outcomes (graft failure, biopsy proven rejection and death) among kidney transplant recipients.

Methods: We perform a retrospective study of 2064 patients who received a kidney at our center between 2010 and 2017. Patients were stratified according to recipient/donor CMV serology status at the time of transplant. Donor and recipient demographics, incidence of organ rejection, graft failure, patient mortality, CMV infection after transplant (early and delayed onset) and renal function were determined using the electronic transplant database at our institute. CMV infection was defined as evidence of CMV replication (viremia) regardless of symptoms, and CMV syndrome was defined as the presence of 1 or more of the following, together with evidence of CMV viremia: fever (>38°C), new malaise, leukopenia (<3500/μL), thrombocytopenia (<150,000/μL), or elevation of hepatic transaminases.

Results: Table 1 shows recipient demographics stratified by D/R CMV serology status. D+/R- recipient group was less likely to be diabetic compared to other groups. The mortality rate and the incidence of early and delayed CMV infection were more likely to have confirmed biopsy rejections (Hazard Ratio: 3.2; p= 0.001 & Hazard Ratio: 1.6; p=0.01, respectively); higher risk of mortality (Hazard Ratio: 1.75; p=0.21 & Hazard Ratio: 1.6; p=0.03, respectively) and increased risk of graft failure (Hazard Ratio: 2.4; p= 0.04 & Hazard Ratio: 1.4; p=0.19, respectively).

Conclusion: On long-term follow-up, CMV infection is more prevalent among seronegative patients who received a graft from seropositive donors (CMV D+/R-). Early and delayed onset of CMV infection or syndrome can adversely affect graft function and patient survival. We need more aggressive prophylaxis and post-transplant screening for high-risk patients. Development of CMV vaccine may help CMV negative recipients in the future.

### Table 1: Recipient Demographics

<table>
<thead>
<tr>
<th></th>
<th>D+ R+</th>
<th>D+ R-</th>
<th>D- R+</th>
<th>D- R-</th>
<th>Total</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>264</td>
<td>559</td>
<td>250</td>
<td>963</td>
<td>2064</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>13.0%</td>
<td>28.0%</td>
<td>12.0%</td>
<td>47.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>38%</td>
<td>46%</td>
<td>55%</td>
<td>46%</td>
<td>44%</td>
<td>0.002</td>
</tr>
<tr>
<td>Black (%)</td>
<td>12%</td>
<td>14%</td>
<td>19%</td>
<td>14%</td>
<td>14%</td>
<td>0.12</td>
</tr>
<tr>
<td>Age at Tx (yrs)</td>
<td>51 ± 15</td>
<td>53 ± 13</td>
<td>52 ± 15</td>
<td>54 ± 14</td>
<td>53 ± 14</td>
<td>0.019</td>
</tr>
<tr>
<td>Diabetic (Yes)</td>
<td>25%</td>
<td>28%</td>
<td>30%</td>
<td>33%</td>
<td>29%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Deceased Donor (%)</td>
<td>33%</td>
<td>50%</td>
<td>69%</td>
<td>74%</td>
<td>64%</td>
<td>0.0001</td>
</tr>
<tr>
<td>CDC High Risk</td>
<td>24%</td>
<td>15%</td>
<td>16%</td>
<td>16%</td>
<td>16%</td>
<td>0.243</td>
</tr>
<tr>
<td>Donor Age (yrs)</td>
<td>42 ± 14</td>
<td>39 ± 17</td>
<td>41 ± 14</td>
<td>41 ± 15</td>
<td>41 ± 15</td>
<td>0.019</td>
</tr>
<tr>
<td>Expired</td>
<td>13.0%</td>
<td>9.0%</td>
<td>18.0%</td>
<td>14.0%</td>
<td>13.0%</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMV Infection 90d post-TX (%)</td>
<td>0.8%</td>
<td>0.3%</td>
<td>3.6%</td>
<td>1.6%</td>
<td>1.3%</td>
<td>0.001</td>
</tr>
<tr>
<td>Odds Ratio</td>
<td>1.0</td>
<td>0.230</td>
<td>4.899</td>
<td>2.180</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>CMV Infection delayed-onset post-TX (%)</td>
<td>3.0%</td>
<td>4.0%</td>
<td>27.0%</td>
<td>7.0%</td>
<td>8.0%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Odds Ratio</td>
<td>1.000</td>
<td>1.410</td>
<td>13.700</td>
<td>2.700</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>
Predictors of Metabolic Syndrome Following One-Year Post Kidney Transplantation Among Vietnamese Patients

Nguyen Thu Ha1,2, Poh Bee Koon1, Zulfiti Azuan Mat Daud2, Rozita Mohd2, Ruzita Abd. Taib1, Ho Trung Hieu4.
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Background: Metabolic syndrome (MS) contributes to excess graft failure and poor survival of kidney recipients and, hence, becomes an important clinical target following kidney transplantation. This study aims to determine factors associated with increased risk of MS events in Vietnamese kidney transplant patients.

Methods: We conducted a single-centre cohort study among 104 patients receiving a first kidney transplant at a hospital in Vietnam. MS was defined according to the criteria of the National Cholesterol Education Program Adult Treatment Panel III and diagnosed after 1-month to 1-year post-transplant.

Multivariable Cox proportional hazards models were applied to detect potential risk factors for MS.

Results: A total of 75 patients completed one-year follow up post-transplantation with 53.3% (n=40) presenting with MS. Mean age of patients was 41.9±11.6-year-old, and the average duration of renal replacement therapy was 27.9±41.1 months. Prevalence of overweight was 4.0%, 69.3% hypertension, 54.7% low HDL-C, 94.7% hypertriglyceridemia, and 89.3% had hyperglycemia. Patients with hyperglycemia and low HDL-C before the transplantation had a significantly higher risk for MS later (OR 4.74, 95%CI 1.60 – 14.06 and OR 7.33, 95%CI 1.40 – 38.34, respectively). In the multivariable Cox proportional hazards, BMI (HR 0.87, 95%CI 0.78 – 0.97; serum calcium (HR 0.15, 95%CI 0.04 – 0.56); serum albumin (HR 1.25, 95%CI 1.12 – 1.40); triglyceride (HR 1.41 95%CI 1.07 – 1.86); blood level of tacrolimus (HR1.15, 95%CI 1.06 – 1.25); and mycophenolate mofetil (HR 1.003, 95%CI 1.002 – 1.005) were associated with increased risk of MS.

Conclusion: Our results suggest that the presence of low HDL-C and hyperglycemia before kidney transplantation, are independent risk factors for MS in Vietnamese kidney transplant patients. MS is associated with BMI, serum calcium, albumin, triglyceride, the high blood level of tacrolimus and dose of mycophenolate mofetil. Interventions aimed at improving these factors before and after the transplantation may reduce the incidence of metabolic syndrome.

HLA Desensitization in Kidney Transplantation

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1L.N.Gumilyov Eurasian National University, Nur-Sultan, Kazakhstan; 2Scientific and Production Center of Transfusiology, Nur-Sultan, Kazakhstan; 3National Research Oncology Center, Nur-Sultan, Kazakhstan; 4Astana Medical University, Nur-Sultan, Kazakhstan.

Introduction: In the last decade, organ transplantation has been developing fast in Kazakhstan. 1892 transplants have been performed since 2012. Patients often need kidney (91.5%), heart (4.4%), liver (4%) transplantations. Nearly 100 kidney transplantations from living donors and 30 ones from deceased donors are performed annually. The most important factor hindering the long-term survival of recipients is HLA sensitization. The formation of specific antibodies to HLA may develop as a result of previous transplantation, blood transfusion or pregnancy. There are 3.5% highly sensitized patients among 3012 patients on the waiting list for kidney transplantation. This study aimed to review an effectiveness of desensitizing therapy during the preparation of patients for transplantation.

Methods: This study included 13 patients with end-stage chronic kidney disease (CKD). The participants underwent a general clinical examination, a specialized immunological study to determine the level of antibodies to leukocyte antigens (anti-HLA) before and after the desensitization stages. Microsoft Excel was used to perform statistical analyses. Qualitative variables were summarized in the form of absolute frequency and percentages.

Results: The proportion of male and female was 38.5% (5) and 61.5% (8), respectively. The average age of the participants was 44.8 years, ranging from 25 to 58 years. 30.8% (4) of patients had a decrease in the level of leukocyte antibodies after rituximab administration and three sessions of citrate plasmapheresis. In 23.1% (3) of patients, the level of sensitization remained the same. An increase in the level of leukocyte antibodies was observed in 15.4% (2) of participants. 15.4% (2) of patients are currently at the second stage of desensitization. In 53.8% (7) of patients, a positive cross-match test is observed, which leads to the impossibility of kidney transplantation from living donor. A significant decrease in leukocyte antibodies was revealed in 53.8% (7) patients after repeated plasmapheresis sessions, despite the absence of differences in the level of antibodies after administration of rituximab and one plasmapheresis session. 46.2% (6) of the participants underwent only the first stage (rituximab) and one plasmapheresis session. 37.5% (3) of female had 5 or more pregnancies, which affects the increased immunological risk in CKD. 62.5% (5) of women had one pregnancy each and they had a decrease in the level of antibodies after rituximab and one plasmapheresis session. One patient has a significant decrease in the level of leukocyte antibodies after several sessions of plasmapheresis. 25% (2) undergo the first stage of desensitizing therapy.

Conclusion: According to preliminary data, the combination of plasmapheresis and rituximab was insufficient to achieve a negative cross-match test and kidney transplantation. In this regard, we recommend adding the introduction of human immunoglobulin to desensitizing therapy. This study is ongoing.
Development of Post-transplant Malignancy in Kidney Transplant Recipients

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Introduction: Malignancy constitutes a major cause of death in kidney transplant recipients and its incidence is rising around the world. We aimed to study the incidence of de novo malignancies, their management, and patient outcomes.

Method: We extracted data on de novo malignancies in patients who received a kidney transplant from a living or a deceased donor in our center between 1/1985 and 12/2020. Out of 2,509 recipients, we identified 221 patients, who developed 227 malignancies in a median time of 94 (IQR 40-170) months after transplantation. Among them, 60% were male and the median age at transplantation was 49 (IQR 38-59) years. Immunosuppression was modified on the basis of cancer type, stage, treatment options, and immunologic risk. Initial immunosuppression was maintained in 82 (42%) patients who were diagnosed with end-stage cancer.

Results: Most frequent malignancies were lung cancer (16%), post-transplant lymphoproliferative disease (PTLD, 15.4%) and Kaposi sarcoma (9%). The cumulative incidence of PTLD was 1.37%. Incidence rates of malignancies in 5, 10, 20 years after transplantation were 2.8%, 4.7%, and 7.2% respectively. In a median time of 20 (IQR 6-56) months after a cancer diagnosis, 127 (56%) patients died, 123 of them because of cancer. Mortality relative risk was higher, compared with the general population (SMR 3.3). Nine (9%) patients developed a rejection episode and 22 (23%) lost their graft in a median time of 23 (IQR 7-47) months after diagnosis. The 5- and 10-year cancer-related survival of those with functioning graft was 51% and 45% respectively.

Conclusion: Kidney transplant recipients are at high risk of developing malignancies and outcomes are worse compared to the general population.

Multicentre Study on Transplantation Access and Outcome in Patients Undergoing Hemodialysis in TANKER Charity Dialysis Units – An Observational Study From South India

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Introduction: Chronic kidney disease (CKD) with its ever-increasing prevalence, morbidity and mortality, is an important public health problem world-wide. Over half the patients with eGFR < 15ml/min/1.73m2 have this degree of CKD at initial doctor visit itself. Over 90% requiring RRT soon die due to unaffordability despite costing only a fraction of that of developed countries. Over 60% of those starting RRT stop due to financial difficulty and few, if ever undergo kidney transplantation.

Patients and Methods: We looked at patients with End Stage Kidney Disease on hemodialysis at Tamilnad Kidney Research (TANKER) Foundation charity dialysis units that have thus far offered free or subsidised dialysis for over 2000 patients over nearly 3 decades of service, looking at those who were able to undergo kidney transplantation.

Results: A total of 43 patients underwent kidney transplantation, most of them at the state capital city of Chennai (28 patients, 65.12%). Most patients were 36.74 ± 10.23 years with the youngest being 16 years old and the oldest 63 years old. Nearly 70% of recipients were male. The mean duration of dialysis pre-transplantation was 1052.16 ± 774.27 days, i.e. nearly 3 years. The longest dialysis vintage was nearly 7 and a half years. 51.2% of the transplant surgeries were done in government hospitals where the state funds the costs of surgery and more than 60% were deceased donor transplantations (27 of 43). Over a quarter (12, 27.9%) had graft loss whereas one patient died with a functioning graft. Over half the transplant recipients are alive (23, 53.49%), 6 recipients (13.95%) had died and the rest (14, 32,56%) were lost to follow up.

Conclusions: Successful kidney transplantation is possible even in resource poor settings with helpful and magnanimous donations of donors, due to whose help several have lived successfully on hemodialysis and some have undergone kidney transplantation. More than half the recipients are alive, though a considerable number are lost to follow-up.
P8.151

Serum Klotho and FGF-23 Levels and Their Variability Within Two Years After Kidney Transplantation

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1Nephrology, Regional University Hospital (IBIMA), REDinREN (RD16/0009/0006), Malaga (España), Málaga, Spain; 2Nephrology, Instituto de Investigación Sanitaria de la Fundación Jiménez Díaz, Universidad Autónoma de Madrid., Madrid, Spain; 3Immunology, Regional University Hospital (IBIMA), REDinREN (RD16/0009/0006), Malaga (España), Málaga, Spain; 4Pathology, Regional University Hospital (IBIMA), REDinREN (RD16/0009/0006), Malaga (España), Málaga, Spain.

Purpose: Klotho is a protein produced in renal tubular cells with nephroprotective actions which acts as a co-receptor for phosphaturic factor FGF-23. The natural history of the production and expression of post-transplant klotho and FGF-23 is still unknown. Our aim is to know the evolution of these molecules during two years after kidney transplant (KT).

Methods: Klotho and FGF-23 levels were determined in 42 patients at baseline, third and twenty-fourth month after kidney transplant (KT), measured by ELISA. The glomerular filtration rate (GFR) of the kidney graft was performed by indirect methods (formula:MDRd and CKD-EPI) at each study visit.

Results: A total of 146 kidney transplant patients were included in the study and 42 patients have completed the follow-up. The clinical and demographic characteristics of donor and recipients are shown in Table 1. Klotho levels at the third month decreased significantly in both groups (basal 452.69±236.85 vs third month 408.83±223.34; p=0.01) rising in month 12 (523.9±279.6), remaining at these values in the second year after KT (511.1±308.3), even higher than before KT. Similarly, when we analyzed the pre-transplant FGF23 in 56 patients, we observed a reduction trend at the third month, which was maintained until 24 months (baseline 783 vs 193.88 at third month, 158.32 at month 12 and 192.10 in month 24; p=0.066).

Conclusions: We describe a decrease in Klotho levels which increase after one year post KT, which could be justified by the "stunned" of the renal tubule after KT, caused by ischemia-reperfusion time, tubular necrosis, treatment with calcineurin inhibitors, which improves and rises to levels even higher than those prior to KT. More prospective studies are needed to confirm these hypotheses.
Clinical Characteristics and Factors Related to Recurrent Cytomegalovirus Infection Post-kidney Transplant in Adult Patients at Cho Ray Hospital

1Tropical disease department, Cho Ray hospital, Ho Chi Minh, Viet Nam; 2Nephrology Surgery department, Cho Ray hospital, Ho Chi Minh, Viet Nam.

Objective 1: Cytomegalovirus (CMV) is one of the main causes of opportunistic infections after kidney transplantation. Manifestations of CMV disease in post renal transplantation patients are quite discreet, non-specific and difficult to diagnose early. Asymptomatic recurrent CMV infection has been reported remarkably to increase mortality rate and rejection incidence, and effect on graft survival. The recently follow-up and treatment procedures’ changes make it urgent to re-evaluate the incidence and the factors related to the risk of CMV recurrence as well as the clinical characteristics of CMV infection in postkidney transplantation patients. This helps to control the recurrence of CMV infection as well as to diagnose CMV disease early and treat it promptly and appropriately to reduce the mortality rate of patients after transplantation.

Method: Objective 1: Retrospective cohort study of adult renal transplant recipients between January 1, 2015 and December 31, 2018. Objective 2: A cross - sectional descriptive study on 22 cases of CMV disease in post kidney transplant patients to present a review of the main clinical aspects of cytomegalovirus infection in renal transplants with a focus on clinical approach and its future perspectives.

Results: Objective 1: A total of 365 patients who received a renal transplant at Cho Ray hospital in the study time period were reviewed for the presence of CMV infection occurring less than 540 days after transplant. The recurrent CMV infection was observed in 254 cases (69,6%), but only 3 patients (0,8%) developed CMV disease. Independent risk factors of CMV infection were HLA infection was observed in 254 cases (69,6%), but only 3 patients (0,8%) developed CMV disease. The appropriate dose of immunosuppressants plays an important role in the prevention of recurrent CMV infection and the successful treatment of disease due to it.

Objective 2: Male majority (2/3), with average age of 47,5 ± 4,5. Rate of symptomatic recurrence CMV infection in the first 6 months, 6 - 12 months, 1 - 5 years, 5 - 10 years after transplant were 45,4%, 9,1%, 27,3% and 18,2% respectively. Common clinical manifestations are fever 59,1%, respiratory, renal and gastrointestinal manifestations 31,5%, 27,3% and 13,6%, respectively. Two cases of CMV retinitis with typical fundus lesions were treated with intraocular Ganciclovir, however, vision was not fully recovered. Lymphopenia <1.000 cells/mm3 was observed in most cases of CMV disease after kidney transplantation. Quantitative PCR of CMV DNA in plasma ranged from 375 – 6.533,850 copies/mL, 6 of 22 cases of PCR CMV DNA in plasma >4.000 copies/mL, of which 5 severe cases developed rapidly progressive respiratory failure and 2 deaths.

Conclusion: Recurrent CMV infection has a high rate in adult patients after kidney transplantation, so it is necessary to take initiative for screening, monitoring and treating early to reduce mortality and protect the transplanted kidney. The appropriate dose of immunosuppressants plays an important role in the prevention of recurrent CMV infection and the successful treatment of disease due to it.

Key words: Cytomegalovirus, Kidney transplantation, Post-transplant infection.

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A Nomogram for Predicting BK Virus Activation in Kidney Transplantation Recipients Using Clinical Risk Factors

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BK virus is a common opportunistic viral infection that could cause BK virus-associated nephropathy in renal transplant recipients. Thus, we retrospectively analyzed clinical and laboratory data associated with higher risk of BK virus activation from 195 renal transplant recipients by multivariable logistic regression and performed the external validation. Results showed that the patients with BK virus active-infection were associated with deceased donor, had lower direct bilirubin levels, higher proportion of albumin in serum protein electrophoresis, lower red blood cell and neutrophil counts. Multivariate logistic regression analyses revealed that the living donor, direct bilirubin, neutrophil counts were significantly associated with BK virus activation. The logistic model displayed a modest discriminability with area under receiver operating characteristic curve of 0.689 (95% CI, 0.607–0.771; P < 0.01), and also demonstrated a good performance in the external validation data-set (area under receiver operating characteristic curve was 0.699, 95% CI: 0.5899 - 0.8081). The novel predictive nomogram achieved a good prediction of BK virus activation in kidney transplant recipients.

Current Trends in Anemia Treatment in Kidney Transplant Recipients

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Background and Aims: The topic of management of chronic kidney disease (CKD) anemia has constantly been improving. This study aimed to assess the prevalence and current trends in anemia treatment in real-world kidney transplant recipients (KTR).

Methods: This cross-section study included 509 KTR patients, mean age – of 53 years, 51.5% male, with functioning grafts in the late post-transplant period in the last quarter of 2021, in an average of 9.4 years post-transplantation. Data were analyzed using SPSS Statistics 27.0. Student’s t-test, Chi-squared test, Pearson correlation tests were used. According to the Kidney Disease: Improving Global Outcomes (KDIGO) definition, anemia was determined as a hemoglobin (Hb) level of <120 g/L for women and <130 g/L for men. CKD stage was determined by the estimated glomerular filtration rate (eGFR) calculated using creatinine in the CKD-EPI equation.

Results: The prevalence of anemia in the KTR population was 35% (n=178), increasing from 13% to 96% by progressing CKD from stage 1 to 5 in a transplant (Table 1: The prevalence of anemia depends on the stage of CKD in a transplant.). A moderately strong Pearson correlation was recognized between the stage of CKD and anemia (r=0.441; p<0.001). A statistically significant association (p<0.001) was detected between anemia and the female gender (n=107; 60% of all anemic patients). We found no significant association between anemia and the use of mycophenolate or calcineurin inhibitors. Still, there was a statistically significant association between steroid use and anemia (p=0.041), with a 31% (Odds Ratio = 0.69) less chance of anemia in a group that received steroid therapy. 90% of anemic patients had normochromic, normocytic anemia, 7.8% hypochromic, microcytic, and 2.2% hyperchromic, macrocytic anemia. The treatment involved iron replacement in 29% (n=51) of patients, of whom 92.2% had oral medication and 7.8% intravenous. 54% (n=96) of anemic KTR received treatment with erythropoiesis-stimulating agents (ESAs): 27.1% with darbepoetin alfa and 72.9% with methoxy polyethylene glycol-epoetin beta. Anemia was corrected up to Hb level >110 g/L in 69.7% (n=67) of ESAs receiving KTR. A statistically significant correlation was not detected between the ESAs dosage (µg/kg) and the correction of the anemia (p=0.217).

Conclusion: Like in the general CKD population, the prevalence of anemia in KTR increases as CKD progress in a transplant. The extent of anemia correction seems insufficient, although it includes both major components: iron replacement and ESAs. We found anemia more prevalent in female patients and those not receiving steroids in the immunosuppressive regimen. This last unexpected finding needs further exploration.
The Unfavorable Influence of Oral Health on Pre-kidneytransplant Patients’ Quality of Life

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Introduction: In order to perform kidney transplantation (KT), there is a need for interprofessional health action in the recipient’s preparation and adequacy. One of the important prerequisites for greater chances of success in KT is these individuals’ oral health, which reduces the risk of odontogenic and secondary infections during and after transplantation. Furthermore, the state of one’s oral health has an impact on one’s overall quality of life, which can jeopardize the recipient of KT.

Aim: The goal of this study was to assess the oral health of pre-transplant patients and its impact on quality of life.

Method: Pre-RT patients were examined and a convenience sample was used in this cross-sectional investigation. To assess the impact of oral health, the following variables were assessed: dental caries activity (DMFT), oral dental plaque index (PI), gingival bleeding index (GBI), dental calculus, periodontal pocket depth 4-5mm, gingival index (GI), upper denture use (UDS) and lower denture use (LDU), need for upper denture use (NUDU) and need for lower denture use (NLDU), tongue coating index (TCI), halitosis, the presence of tongue coating, hypoplasivation, and the OHIP-14 questionnaire were used to assess the impact of oral health on quality of life, and the results were analyzed using descriptive statistics.

Results: The results showed that a total of 14 people (100%) were evaluated, with an average age of 49.64 ± 13.35 years. We discovered mean values of 1.07 for GBI, 1 for dental calculus, 0.71 for periodontal pocket depth between 4-5 mm, 0.56 for GI, 0.79 for UDS and LDU, 1.21 for NUDU, and 1.14 for NLDU for the analyzed variables. The individuals had at least one decaying, lost, or filled tooth (DMFT) and dental plaque, with high mean values of 7.64, 20.5, and 1.8. All of the participants exhibited tongue coating and oral halitosis (sulfide), as well as 8 (57.14%) hyposalivation, which increased the risk of oral opportunistic infections. In all dimensions assessed, the impact of oral health on quality of life was negative, ranging from weak to moderate, and the sum of the dimensions had a moderate total impact.

Conclusion: Pre-transplant patients have poor oral health, which has a negative impact on their quality of life, particularly in terms of salivary flow and the risk of oral opportunistic infections. These findings show that pre-KT oral adequacy support from the interprofessional transplant team is required. This study was approved by the Research Ethics Committee of the institution where it was carried out (CAEE 71651517.9.000.5417). Center of Clinical Research of Bauru School of Dentistry of University of São Paulo, Bauru State Hospital.

Impact of the Pandemic on Liver Transplantation and Use of Telemedicine – Clinical Hospital UNICAMP

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Introduction: The covid-19 pandemic has led to changes in the care of transplant patients, including authorization from the SNT/MS/Brazil for its use since April 2020.

Objective: To assess the impact of COVID-19 on kidney and liver transplantation and the use of telemedicine.

Method: To verify the number of visits, number of transplants, types of assessments, incidence of COVID-19 in transplant recipients, use of immunosuppression, and impact on the number of transplants, descriptive statistics were used.

Result: A specific TCLE was implemented for the pandemic season, tele-guidance and teleconsultations were carried out institutionally with medical, nursing, psychology, and social assistance assessments, the return frequency changed thanks to the 6-month LME (saving in TFD about 20 thousand/patient). 4,000 consultations were carried out in 2020, with a 50% drop in face-to-face consultations (4 outpatient clinics/week) with directed aramnisis, the sending of images and outpatient results was done by institutional email as well as renewal of the MELD (for patients in list). There was a 25% reduction in the number of transplants (lack of an ICU bed and patient refusal due to fear/fee), a 50% drop in the number of patients enrolled in the list. The immunosuppression adjustment was mainly performed in the second wave (November 2020 to March 2021). We observed 30 COVID cases in 750 follow-up liver transplants and 100 cases in 3000 follow-up kidney transplants. In liver transplantation the mortality was 25% and in kidney transplantation it was 26%. The most frequent comorbidities were age > 60 years, presence of diabetes and time greater than ten years after transplantation. 2 patients with COVID-19 and 2 with kidney transplants were transplanted with liver, which evolved well and there was 1 patient transplanted due to complications after IV/COVID-19 who also evolved well.

Conclusion: COVID-19 had a high impact on transplantation in our service and telemedicine is probably here to stay.
Percutaneous Transhepatic TIPS for Budd-Chiari Syndrome As a Bridge to Liver Transplantation

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Purpose: To evaluate the effectiveness of percutaneous transhepatic direct simultaneous puncture of portal vein and inferior vena cava in Budd-Chiari syndrome and the clinical outcomes.

Material and Methods: From January 2006 to January 2022, we performed TIPS in 65 consecutive patients (mean age, 33 years) with BCS (8 patients with acute BCS and 57 patients with subacute and chronic BCS). Doppler US was performed first day, one week, one month and then 3 months apart. Portography and pressure measurements were performed every year if no shunt dysfunction was detected before. Mean follow-up of 52 months (range, 6 months -119 months).

Results: TIPS procedure was technically successful in all patients. In all patients, bare stents were used. Patients were antiocoagulated with warfarin after TIPS procedure. Early thrombosis (in one week) was diagnosed in 13 (20%) patients and TIPS revision was required. One year primary patency was 65.2%. Clinical success was achieved in 60 patients. 5 patients required TIPS revision was required. One year primary patency was 65.2%. Clinical success was achieved in 60 patients. 5 patients required TIPS revision was required. One year primary patency was 65.2%.

Conclusion: Percutaneous direct puncture of portal vein and inferior vena cava is safe and effective in patients with Budd-Chiari syndrome. This procedure may provide an effective alternative for the management of Budd-Chiari syndrome and the clinical outcomes.

Introduction: Hepatocellular carcinoma is the most common primary liver tumor, with 905,677 cases diagnosed to date, and 830,180 deaths. In Argentina, it accounts for the 9th cause of death for cancer in men and the 10th in women. Unlike other highly-prevalent tumors, scientific evidence for most therapeutic options is limited mainly to small cohorts and retrospective studies. The aim of this study is to characterize and describe epidemiologically patients with diagnosis of hepatocellular carcinoma in the Italian Hospital of Buenos Aires during a 12 year period.

Methods: A retrospective, observational analytical cohort study was performed. All patients over 18 years diagnosed with Hepatocellular carcinoma between January 2007 and December 2018 were included. The study was approved by the institutional ethics committee. Data was obtained from electronic medical records. Patients were diagnosed with HCC using national guidelines until 2011, and LI-RADS system afterwards. patients were staged according to BCLC criteria, and were divided into three different groups according to the treatment: curative intent treatments (surgical resection, liver transplant or radiofrequency ablation), non-curative treatments (Transarterial chemoembolization, transarterial radioembolization, Sorafenib) and palliative treatments.

Results: Overall survival for our cohort was 58%, 46%, and 36% at 1, 3 and 5 years respectively. Average survival for patients receiving palliative treatment was 5 months, while those who received either non-curative or curative treatment was 23 and 75 months respectively. Recurrence-free survival for those patients who underwent a curative treatment was 89%, 76% y 61% at 1, 3 and 5 years. Patients receiving liver transplant had the best RFS, with 98%, 89% and 77% at 1, 3 and 5 years respectively. Out of 400 cirrhotic patients, almost 60% (231 patients) were BCLC A at diagnosis, 147 patients were BCLC B, and 18 patients BCLC C-D. Mean OS for these groups was 39 months, 21 months and 4 months respectively. Of 231 BCLC A patients, 92 patients had Liver transplant performed, and 50 of these required bridging therapies to be eligible candidates for LT. In the BCLC B group, 6 patients had LT performed, previous TACE so as to become eligible candidates. 121 patients presented HCC in a non-cirrhotic liver. 52% of these patients received surgical resection, while 36 patients received some other kind of treatment (TACE, TARE, Chemotherapy, Sorafenib or a combination of these). Follow-up time for these patientses was 35 months.

Conclusions: A thorough analysis of etiology, risk factors, incidence, mortality and treatment was made. Results are in consonance with worldwide reports, showing the applicability of BCLC criteria and management in a high volume center in a developing country. The study’s importance lies in its large sample size, quantity and quality of data, and will most certainly stimulate the development of local studies in hepatocellular carcinoma.
Evaluation of Quality of Life in Adult Patients After One Year Liver Transplantation

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Introduction: Liver transplantation (LT) aims not only to obtain long survival, but also to achieve an excellent quality of life (QOL). The purpose of our study is to assess several QOL aspects of recipients after 1 year of LT and to identify potential factors that might be associated with impaired QOL.

Materials and Methods: Retrospective analysis including LT between 2013 to 2021. The Liver Disease Quality of Life questionnaire (LDQOL 1.0), and the consent form to participate of this study were given personally or sent by e-mail. This questionnaire includes 111 items distributed within 20 domains. Fulminant liver failure, hepatorenal transplantation and underaged patients were excluded. Significance was explored using T tests. Differences were considered statistically significant at p < 0.05.

Results: This study included 89 patients out of 360 LT (56% male) who answered the survey, age range 24.8–75 years (mean: 52.5). On average, the patients had to wait 360 days before undergoing LT. Primary etiologies of liver disease were: hepatitis C virus (22.5%), alcohol (22.5%), autoimmune cirrhosis (22.5%), primary biliary cirrhosis (14.6%), NASH (6.7%), primary sclerosing cholangitis (3.3%), cryptogenic (2.2%), and others (5.6%). Thirty-one LT also presented hepatocarcinoma (HCC). The vast majority (93%) had moderate to severe liver disease, with 46% Child-Pugh B and 47% Child-Pugh C. After 1 year LT, QOL was improved resulting with a mean of 83.69%. The general well-being domain rated lowest with 69%. Higher scores (89-90%) were obtained on effects of liver disease, stigma of liver disease, physical limitations, emotional limitations and loneliness. There was a significant association between the Child-Pugh classification and body pain, emotional well-being, memory and stigma of liver disease (p<0.05). Lower MELD scores (<18) showed better results after 1 year LT in energy/fatigue, emotional well-being, liver disease symptoms, effects of liver disease and hopelessness domains (p<0.05). There was no significant difference when QOL was compared according etiology of chronic liver disease, gender, or age.

Conclusion: After 1 year of LT, patients result on QOL show a significant improvement, even similar to results published on the common population, but also to achieve an excellent quality of life (QOL). The purpose of our study is to assess several QOL aspects of recipients after 1 year of LT and to identify potential factors that might be associated with impaired QOL.

Biliary Complications Following Liver Transplantation: A 13-Years Single-Center Experience

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1-HPB and complex gastrointestinal surgery and abdominal organ transplant, Hospital Universitario Fundacion Favaloro, Caba, Argentina; 2-Hepatology, Hospital ospital ospital osphital Universitario Fundacion Favaloro, Caba, Argentina; 3-Gastroenterology, Hospital ospital ospital osphital Universitario Fundacion Favaloro, Caba, Argentina.

Introduction: Orthotopic liver transplantation (LT) is the chosen treatment for end-stage liver disease. Despite the advances in the surgical techniques, biliary tract complications are the most common problems seen after transplantation with an incidence range of 10-25%. We aim to describe the incidence of biliary complications at our center.

Materials and Methods: Retrospective study of patients who suffered from biliary complications after LT between September 2009 and February 2022 in a single center. Demographic characteristics: cause of liver failure, MELD score, time on waiting list (WL), DRI, national, regional or local procurement; preservation solution, warm ischemia time (WIT), cold ischemia time (CIT), chosen treatment and success rate (SR), patient and graft survival. Biliary complications were divided into 2 groups, according to the moment of appearance: early complication (EC) when they happened within the first 30 post-operative days and delayed complication (DC) when they occurred afterwards. All analyses were performed using IBM SPSS v25.0.

Results: From a total of 549 LT that were performed during the period of study, 90 (16%) had biliary tract complications. Among them, 78 were adult recipients, with a mean age of 48 years old (DS 21). Sixty-four transplants (71%) were performed due to cirrhosis, caused mainly due to viral disease (25, 39%) and alcohol (18, 28%). Sixty-nine (90%) were performed with whole liver and 8 (10%) with partial grafts (7 right and 1 left lobe). The most frequent biliary complication in the EC and DC group was the biliary anastomotic stenosis, with 21 (60%) and 33 cases (78%), respectively. Eighteen patients (23%) lost their graft (7 EC and 11 DC). Table 1 shows biliary complications according to time of appearance and initial treatment chosen.

Discussion: Biliary complications remain a major cause of morbidity, dysfunction, and mortality in liver transplant recipients and continue to be a challenging aspect in the management of such patients. With appropriate management, however, there impact on graft and overall survival could be minimized.
Liver Transplantation for Treatment of Acute Liver Failure After COVID-19 Infection and Anatomopathological Results

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During the year 2019, the world experienced the beginning of a pandemic that has been lasting until the present moment. The liver is one of the organs affected by COVID-19, with transaminase elevations being the most common alteration. Cholestasis is rare, present in less than 1 percent of cases. The aim of this article is to report the case of a 64-year-old male patient with post-COVID cholangiopathy.

C.S.H., male, 64 years old, admitted to a referral hospital for liver diseases and transplants, in Curitiba, Paraná, Brazil. A previously healthy patient, without any history of liver disease or alcohol consumption, with negative serology for viral hepatitis and autoimmune markers, admitted with a prolonged condition of cholestasis associated with hepatocellular dysfunction, evolving with encephalopathy after infection by COVID-19. During hospitalization, three months after infection with the new coronavirus, he developed fulminant acute liver failure according to King’s College criteria. He was included in the list for liver transplantation, persisted without improvement, underwent liver transplantation with an organ from a dead donor and presented good evolution in the postoperative period. Anatomopathological analysis of the explant showed subacute cholestatic liver disease, with involvement of bile ducts and hepatocytes.

Cholangiopathy can be explained by an increased expression of receptors for COVID-19 (ACE-2) on cholangiocytes, which can lead to direct viral damage. Persistent and delayed cholestasis occurs, with elevations of bilirubin and canalicular enzymes, even after recovery of lung function and rehabilitation of these patients, and affects patients without previous liver disease. The main differential diagnosis would be sclerosing cholangitis secondary to critically ill patients (CSCP), due to similar radiological findings. However, the anatomopathological analysis of these patients shows us a new entity, due to the intense presence of cytoplasmic vacuolization of cholangiocytes and microvascular alterations not previously described in (CSCP). This cholangiopathy can lead to progression of liver damage with the potential need for liver transplantation. In the literature review carried out by the researchers in question, four reported cases of liver transplantation for post COVID cholangiopathy were found so far. It is necessary to keep looking on new clinical entities that may arise in the long term, as we become familiar with this new clinical entity.

Hospital Evangélico Mackenzie.
Peri-Hepatic Gauze Packing for the Control of Haemorrhage During Liver Transplantation: Experience of a High-Volume Center

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Introduction: The use of peri-hepatic gauze packing (PHGP) has been rarely reported during liver transplantation (LT). The objective of this technique is to achieve fast control of bleeding while haemodynamic stability is restored and coagulation disorders are fixed. Conditions like baseline cirrhosis-related coagulopathy, intraoperative blood loss, prolonged surgery, anhepatic phase and initial allograft dysfunction may all contribute to persistent bleeding. In some cases, usual means of haemostasis can be ineffective and reiterate attempts at controlling bleeding can be frustrating or even detrimental. Although, PHGP use during LT raises concerns for a potentially increased risk of infection and graft related complications. The aim of our study was to assess the value of PHGP during LT.

Method: We conducted a retrospective and descriptive study. We reviewed the clinical records of 13 orthotopic liver transplantation (OLT) patients undergoing PHGP between a total of 407 patients at the HPB surgery and liver transplant department of the Hospital de Alta Complejidad “El Cruce” between January 2013 and February 2022. Patients and donor’s demographics and intra/postoperative features were analyzed. Continuous data are presented as medians and means and standard deviations. Discrete data are given as counts and percentages. Chi-square test, Fisher exact test, Mann–Whitney U test and Student’s T-test were used when appropriate (for categorical and continuous data respectively). Two-sided p value equal or less than 0.05 was considered to indicate statistical significance with a confidence interval of 95%. All analyses were conducted using MedCalc version 20.027 (https://www.medcalc.org/).

Results: Of 407 recipients, 13 were treated with packing for peri-hepatic bleeding (3.19%). One of them required urgent reoperation for ongoing haemorrhage after PHGP. After that, correction of haemodynamic and coagulation parameters was constantly achieved (table 1). 6 patients died (46.15%), none of them related to the PHGP. Patient survival (table 2) was associated with recipient age (p≤0.001) and intraoperative plasma transfusions (p=0.02).

Conclusion: Peri-hepatic gauze packing it’s highly effective in achieving adequate haemostasis, allowing the correction of haemodynamic parameters and underlying disorders. However, it’s associated with relevant morbidity and high mortality. We believe that PHGP is a valuable strategy in the armamentarium of the liver transplant surgeon facing a life-threatening situation like the persistent bleeding during the operation.

Table 1

<table>
<thead>
<tr>
<th>PHGP patients (N = 13)</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age (years)</td>
<td>51.9 ± 15.1 (24-68)</td>
<td></td>
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<tr>
<td>Main etiology of liver disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcoholic</td>
<td></td>
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<tr>
<td>Cholestatic or autoimmune</td>
<td></td>
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<tr>
<td>Cryptogenic or NASH</td>
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<tr>
<td>Hepatitis C virus</td>
<td></td>
<td></td>
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<tr>
<td>Fulminant hepatic failure</td>
<td></td>
<td></td>
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<tr>
<td>Hepatocellular carcinoma</td>
<td></td>
<td>1.7 (7.7)</td>
</tr>
<tr>
<td>Previous upper abdominal surgery</td>
<td>6 (46.15%)</td>
<td></td>
</tr>
<tr>
<td>Re-Op</td>
<td>1 (7.7%)</td>
<td></td>
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<tr>
<td>Type of graft</td>
<td></td>
<td></td>
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<tr>
<td>Whole liver</td>
<td>12 (92.3%)</td>
<td></td>
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<tr>
<td>Right split</td>
<td>1 (7.7%)</td>
<td></td>
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<tr>
<td>Recipient BMI</td>
<td>28.8 ± 4.91 (20.8-35.9)</td>
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<tr>
<td>MELD</td>
<td>28.84 ± 4.91 (22-39)</td>
<td></td>
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<tr>
<td>Donor age</td>
<td>44.48 ± 13.19 (23-65)</td>
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<tr>
<td>Use of vasoactive drugs for donor maintenance</td>
<td></td>
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<tr>
<td>Yes</td>
<td>6 (46.15%)</td>
<td></td>
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<tr>
<td>No</td>
<td>7 (53.85%)</td>
<td></td>
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<tr>
<td>Microscopic allograft steatosis</td>
<td></td>
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<tr>
<td>Yes</td>
<td>6 (46.15%)</td>
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<tr>
<td>No</td>
<td>7 (53.85%)</td>
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<tr>
<td>Total ischaemia time (min)</td>
<td>476 ± 113 (219-660)</td>
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<tr>
<td>Total anaesthesiologist time (min)</td>
<td>449.9 ± 5.59 (36-60)</td>
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<tr>
<td>Total surgery time (min)</td>
<td>337 ± 61 (180-410)</td>
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<tr>
<td>Intraoperative PRBC transfusions (units)</td>
<td>9 ± 4.08 (5-20)</td>
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<tr>
<td>Intraoperative plasma transfusions (units)</td>
<td>10.69 ± 3.95 (3-25)</td>
<td></td>
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<tr>
<td>Intraoperative platelets transfusions (units)</td>
<td>15.58 ± 10.68 (0-35)</td>
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<tr>
<td>End-procedure lactate (mg/dL)</td>
<td>6.25 ± 2.65 (2.7-11.9)</td>
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<tr>
<td>End-procedure platelets (1000/mm3)</td>
<td>62 ± 87 (26-162)</td>
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<tr>
<td>End-procedure haemoglobin (g/dL)</td>
<td>7.9 ± 1.49 (6.3-12.1)</td>
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<td>Cultures of abdominal samples during removal of PHGP</td>
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<tr>
<td>Yes</td>
<td>2 (15.38%)</td>
<td></td>
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<tr>
<td>No</td>
<td>11 (84.62%)</td>
<td></td>
</tr>
<tr>
<td>Global mortality after LT and PHGP</td>
<td>6 (46.15%)</td>
<td></td>
</tr>
<tr>
<td>Initial failure of the technique</td>
<td>1 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Time of removal of the PHGP (hours)</td>
<td>54 ± 18.09 (24-96)</td>
<td></td>
</tr>
<tr>
<td>Hospital length of stay</td>
<td>17.46 ± 15.59 (1-63)</td>
<td></td>
</tr>
</tbody>
</table>

Data are expressed as frequency (percentage) or mean ± standard deviation. Abbreviations: MELD, model for end-stage liver disease score; PRBC, packed red blood cells.

Table 2

<table>
<thead>
<tr>
<th>Descriptions</th>
<th>Deaths (N = 6)</th>
<th>Alive (N = 7)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microscopic allograft steatosis</td>
<td>4 (66.66%)</td>
<td>2 (28.57%)</td>
<td>0.3</td>
</tr>
<tr>
<td>MELD</td>
<td>11 ± 6 (4-19)</td>
<td>27.42 ± 19 (22-25)</td>
<td>0.18</td>
</tr>
<tr>
<td>Age</td>
<td>46 ± 14 (24-64)</td>
<td>56.4 ± 15.31 (27-47.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative hemodilatation</td>
<td>3 (50%)</td>
<td>3 (42.86%)</td>
<td>0.8</td>
</tr>
<tr>
<td>Days of post-op mechanical ventilation</td>
<td>11 ± 5 (2-23)</td>
<td>22.85 ± 19.05 (9-63)</td>
<td>0.18</td>
</tr>
<tr>
<td>Donor age</td>
<td>46 ± 12 (28-62)</td>
<td>42.9 ± 14 (23-65)</td>
<td>0.66</td>
</tr>
<tr>
<td>Days of donor mechanical ventilation</td>
<td>2 ± 1 (1-4)</td>
<td>3.42 ± 2.2 (1-7)</td>
<td>0.24</td>
</tr>
<tr>
<td>Use of vasoactive drugs for donor maintenance</td>
<td>3 (53.33%)</td>
<td>4 (57.14%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Total ischaemia time (min)</td>
<td>468 ± 116 (342-660)</td>
<td>483 ± 119 (239-551)</td>
<td>0.32</td>
</tr>
<tr>
<td>Total surgery time (min)</td>
<td>342 ± 37 (300-392)</td>
<td>330 ± 78 (180-410)</td>
<td>0.7</td>
</tr>
<tr>
<td>Total anaesthesiologist time (min)</td>
<td>44 ± 11 (27-60)</td>
<td>45.42 ± 8.97 (30-58)</td>
<td>0.85</td>
</tr>
<tr>
<td>Intraoperative PRBC transfusions (units)</td>
<td>10 ± 5 (5-20)</td>
<td>7.85 ± 2.64 (6-13)</td>
<td>0.39</td>
</tr>
<tr>
<td>Intraoperative platelets transfusions (units)</td>
<td>20 ± 11 (0-35)</td>
<td>11.14 ± 8.7 (2-36)</td>
<td>0.13</td>
</tr>
<tr>
<td>Intraoperative plasma transfusions (units)</td>
<td>15 ± 6 (7-25)</td>
<td>7.28 ± 3.35 (5-13)</td>
<td>0.02</td>
</tr>
<tr>
<td>End-procedure lactate (mg/dL)</td>
<td>9 ± 1 (4-12)</td>
<td>8.04 ± 1.91 (6-14.12)</td>
<td>1</td>
</tr>
<tr>
<td>End-procedure AST (U/L)</td>
<td>3164 ± 2016 (997-6505)</td>
<td>2469 ± 1607 (718-4183)</td>
<td>0.51</td>
</tr>
<tr>
<td>End-procedure ALT (U/L)</td>
<td>1122 ± 603 (386-2092)</td>
<td>926 ± 579 (27-3266)</td>
<td>0.56</td>
</tr>
<tr>
<td>End-procedure lactate (mg/dL)</td>
<td>7 ± 1 (3-10)</td>
<td>7.1 ± 2.64 (3.6-11.9)</td>
<td>0.23</td>
</tr>
<tr>
<td>End-procedure platelets (1000/mm3)</td>
<td>46 ± 19 (26-71)</td>
<td>71 ± 43 (28-162)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Data are expressed as frequency (percentage) or mean ± standard deviation and range. Abbreviations: MELD, model for end-stage liver disease score; PRBC, packed red blood cells; AST, Fisher exact; Mann–Whitney U test and Student’s T-test were used when appropriate.
Abstracts

P9.10

Mono-Maintenance Therapy With Anti-icam-1 Monoclonal Antibody Induced Long-term Liver Allograft Survival in Nonhuman Primates

Dongkyu Han1,2, Gwangmin Lee1,2, Joon Young Jang3, Suk Kyun Hong2, YoungRok Choi3, Jae-Ill Lee1, Kyung-Suk Suh3, Nam-Joon Yi3, Jaeseok Yang2.

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Introduction: MD-3 is an anti-human intercellular adhesion molecule-1 (ICAM-1) monoclonal antibody (mAb) that can induce tolerogenic myeloid cells and donor-specific T cell unresponsiveness rather than adhesion inhibition. In a previous study, we demonstrated that short-term (3 months) therapy of MD-3 effectively suppressed liver allograft rejection and thereby prolonged liver allograft survival in nonhuman primate (NHP) models; however, liver allografts experienced chronic rejection later and subsequent graft failure. Based on these promising data, we aimed to investigate whether MD-3 can replace toxic calcineurin inhibitors as a maintenance therapy.

Methods: We used a rhesus macaque liver transplantation model and compared three groups - no immunosuppression group (n = 2), conventional immunosuppression group (n = 4), and MD-3 group (n = 4). Conventional immunosuppression consisted of 2 months of corticosteroid, 3 months of advagraf, and 4 months of mTOR inhibitor. MD-3-based immunosuppression consisted of conventional triple immunosuppression and 13 doses (8 mg/kg/dose) of MD3 for the initial three months, followed by monthly maintenance MD-3 dose after 3 months. Protocol liver biopsy was performed at 4 months, 12 months, 16 months, and 24 months after transplantation.

Results: No immunosuppression control group showed severe acute allograft rejection and showed very short survival (survival duration: day 5, day 6). Conventional immunosuppression group showed acute or chronic allograft rejection and all lost liver allograft by day 66 (survival duration: day 36, 52, 62, 66). One member in the MD-3 group lost liver allograft on day 118 due to liver cirrhosis that was related to hepatic venous obstruction. The other three members in the MD-3 group kept liver allograft on day 118 due to liver cirrhosis that was related to hepatic venous obstruction. The other three members in the MD-3 group kept liver allograft well until now (day 501, 564, 998). One member in the MD-3 group showed mild abnormality in liver function test and mild acute T-cell-mediated rejection on protocol biopsies. The other two live members showed normal liver function test results and no evidence of rejection on protocol biopsy. When we checked MD-3 trough levels, MD-3 levels during the initial two months were lower in the member that experienced mild rejection, compared to the other members of MD-3 group.

Conclusions: Long-term MD-3 mono-maintenance therapy suppressed liver allograft rejection and kept liver allograft survival without maintenance of conventional immunosuppressants including calcineurin inhibitor. Therefore, MD-3 is a promising as a mono-maintenance therapy without calcineurin inhibitors for liver transplantation, although MD-3 failed to induced liver allograft tolerance as a short-term therapy.
Survival of Liver Transplant Patients From 2010 to 2022 Belonging to the Public Financing Program of CUCAIBA As an Institution of the Ministry of Health of Buenos Aires Argentina

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Introduction: Liver transplantation is the therapy of choice for patients with end-stage liver disease, which has been shown to improve life expectancy and quality of life. Currently, the long-term survival of liver transplant recipients under the public financing program of CUCAIBA as an institution of the Ministry of Health of Buenos Aires province in Argentina, is unknown. The objective of this work is to determine the overall survival, at one year and at 5 years, of the patients transplanted under the Transplant Financing Organism Program (EFTO). Secondly, to determine the causes that leads to liver transplantation as well as its relationship with long-term mortality.

Method: All transplant patients from 2010 to 2022 belonging to the EFTO were included in the analysis. Retrospective data analysis was performed. The data were obtained using the database of the National Procurement and Transplant Information System of Argentine (SINTRA), the National Registry of Persons (RENAPER), and the CUCAIBA Drugs Program (PROMECU). All the data collected were checked by telephone with the patients included in the analysis.

Results: 202 liver transplants performed from 2010 to 2022 were included in the analysis. The average age was 39 years with a range of 0 to 65 years. The distribution by sex was 55.9% men and 44.1% women. After the analysis, an overall survival of 60.4% was obtained. Survival at one year was 77.7% and 49.6% at 5 years. Although it is beyond the scope of this study, the results indicate that unknown cirrhosis, 20% in fulminant liver failure, 17.5% in cirrhosis alcoholic, and 12.5% in unknown cirrhosis, remain for future analyses, which affect the sample in the long-term result.

Conclusion: Overall and long-term survival in post-liver transplant patients under the CUCAIBA Transplant Financing Organism Program (EFTO) was 60.4%, 77.7% at one year and 49.6% at 5 years. Although it is beyond the objectives of this work to analyze the causes of mortality, the impact of the causes of this vulnerable population of socio-economic level, the degree of illness they present and the lack of access to medical check-ups, among others, remains for future analyses, which affect the sample in the long-term result.
P9.13
Outcomes in Pediatric Recipients of Living Donor Liver Transplantation
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1Pediatric Hepatology and Pediatric Liver Transplant Section, Hospital Universitario Austral, Pilar, Argentina; 2Hepatic and Liver Transplant Surgery Unit, Hospital Universitario Austral, Pilar, Argentina; 3Pediatric Inpatient Unit, Hospital Universitario Austral, Pilar, Argentina; 4Pediatric Intensive Care Unit, Hospital Universitario Austral, Pilar, Argentina.

Background: Living Donor Liver Transplantation (LDLT) is an option increasingly used to solve deceased organs shortage for pediatric patients with end stage liver disease (ESLD), inborn metabolic diseases or liver tumors.

Aim: To report our results in pediatric patients with LDLT.

Patients and Methods: Digital charts of pediatric recipients of LT between 2001 and 2021 were retrospectively reviewed and outcomes in survival, complications and hospitalization time were analyzed with SPSS program, comparing LD and deceased donor (DD) LT.

Results: 217 pediatric patients received LT between 2001 and 2021 in our center, 37.8% boys and 62.2% girls. Median age at LT was 15mo (range: 28d-17yr). Biliary Atresia was the most frequent indication of LT (56.7%), followed by Acute Liver Failure (18.4%), followed by Acute Liver Failure (18.4%). Median follow-up time was 23mo (range 12mo-18yr). Overall patients and graft survival was 80% and 74%, respectively, improving to 90% and 83%, respectively since 2010, when LDLT increased from 46% to 83% (fig). Overall, 148 patients received LDLT (68.2%) and 69 DDLT. Patients and grafts overall survival was better in LDLT group (84%, 78%, respectively) than in DDLT group (72.5%, 68%, respectively), vascular complications were 18% in LDLT (mostly portal vein stenosis. Hepatic artery thrombosis –HAT: 3%) and 8.7% in DDLT (HAT: 5%), biliary complications were 34% in LDLT and 26% in DDLT, median ICU stay was 6d (range 1-78d) in LDLT and 6d (range 0-117d) in DDLT, median global hospitalization time was 17d in LDLT (range 1-132d) and 16d (range 5-144d) in DDLT, median age at LT was 14mo (range 28d-14yr) in LDLT group and 9yr (range 6mo-17yr) in DDLT group.

Conclusions: In our series, even though LDLT group showed more vascular and biliary complications related to younger and smaller recipients in this group, they had better survival and similar ICU and global hospitalization time. LDLT is an excellent option and provides good outcomes for pediatric patients with ESLD in the scenario of organs scarcity.

P9.14
Massive Blood Transfusion: Risk Factors and Consequences
Alberto Marcacuzco Quinto1, Clara Fernandez Fernandez1, Blanca Toremen1, Oscar Caso1, Jorge Calvo1, Alejandro Manrique1, Álvaro García Sesma1, Carmelo Loizán Segurola1, Carlos Jimenez Romero1, Iago Justo Alonso1.
1Unit HPB and Liver transplantation, 12 de Octubre Hospital, Madrid, Spain.

Introduction: Massive blood transfusion (MBT) is a common occurrence in liver transplant patients. Recipient-related risk factors include cirrhosis, history of multiple surgeries and suboptimal donors. And, while advances in surgical techniques, anaesthetic management and graft preservation have decreased the need for transfusions, this complication has not been completely eliminated.

Materials and Methods: One thousand four hundred and sixty nine liver transplants were performed at our institution between May 1998 and December 2019, and data was available regarding transfusion for 1469 of them. We divided the patients into two groups, with regards to transfusion of 6 or more units of packed red blood cells in the first 24 hours post transplant, and we analyzed the differences between the groups. We analyzed the risk factors for massive transfusion, as well as factors that influence patient survival by using Cox regression.

Results: Out of the 1198 patients, 607 (50.7%) met criteria for massive transfusion. Both groups were statistically different with regards to hepatocellular carcinoma, autoimmune cause, liver/kidney transplant, uDCD, retransplantation, albumin serum levels, creatinine, sodium, bilirubin, haemoglobin, platelets, INR, MELD, McCluskey and Child scores. Out of the variables from the McCluskey index, only the following were significant for massive bleeding: Haemoglobin <10, INR >2 and creatinine >1.2. We contrasted the efficiency of all of the previously mentioned scores for capacity to predict massive transfusion, but none reached an area below the curve above 0.7. Survival was statistically lower at 1, 3, and 5 years when comparing the groups that had MBT compared to those that did not (92.6%, 85.2% and 79.7% respectively in the non MBT group, vs. 78.1%, 71.6% y 66.8% respectively, in the MBT group). Regarding survival analysis, MBT was associated with a 1.5 mortality risk as opposed to no MBT.

Conclusion: Massive blood transfusion impacts patient survival in a statistically significant way. The most significant risk factors are preoperative haemoglobin, INR and creatinine.
What About the Heroes? Living Donor Liver Outcomes, From a Single Latin-American Center Experience Between 2009-2022

Leonardo Montes1, Dario Teran Dr1, Andres Fraile Dr1, Florencia Fernandez Dra.1, Valeria Descalzi Dra.1, Laura Reyes Toso Dra.1, Pablo Farinelli Dr1, Pablo Barros Dr1, Gabriel Gondolesi Dr1.

Objective: To report the long term outcomes of living donor liver transplantation (LD), showing the impact of the protocol used, in order to reduce the mortality in the waiting list.

Background: The shortage of organs favors the need for considering the use of living donor's grafts (LD) for liver transplantation (LT). Reports on long term donor outcomes are scarce. Our aim was to report the long term postoperative outcomes of all LD done in our center.

Materials and methods: Retrospective observational study from 41 consecutive LD surgeries performed between 2009 and 2022 in a single center. Variables included: donor (D) demographics, transplant indications, D-Recipient relationship, type of transplant, surgical approach, type of graft, operative time, days in ICU, length of hospital stay, graft weight, estimated volume, graft/weight ratio (GRWR), postoperative complications using the Dindo- Clavien (DC) classification and mortality. As part of the evaluation, liver anatomy and volumetric assessment was done using CT-Scan and MRI. Biliary anatomy was studied with intraoperative cholangiography. Parenchymal transection was performed using CUSA. Statistical analyses were performed using SPSS v20.0.

Results: Twenty four patients (58%) were woman. The mean donor age was 30±7 years. Transplant indications were biliary atresia (N: 19, 46.3%), Alagille’s syndrome (N: 5, 12.2%), fulminant liver failure (N:5, 12.4%), primary biliary cholangitis (N:4, 9.8%), cryptogenic cirrhosis (N:2, 4.9%), colorectal CA liver metastasis (N:1, 2.4%), and others (N:5,12%). In 63% of cases the donors were parents, figure. Type of transplant was Adult-Pediatric (N: 35, 85%) and Adult-Adult (N: 6, 14%). Open surgery was used in (N: 38, 92%); using median laparotomy in 80% of cases (N: 33), 3 were hand assisted. Types of graft were: left lateral seccionectomy (N: 27, 66%), left lobe (N: 11, 26%) and right lobe (N:3, 8%). The median operative time was 302 (130-570) minutes. Mean graft weight was 309±177 grs, while the mean graft estimated volume calculated with the preoperative CT-Scan was of 342±174gr. Mean GRWR was 2.8±2. The overall complications rate was 12% (N: 5); minor complications were: intra-abdominal collections (N: 2, 4.9%; DC: IIIb; IIa and I), biliary fistula (N: 1, 2.4%; DC: I); while major complications were: one hemoperitoneum (DC IIIb) and one pyloic syndrome (DC IVa); all occurred within the first 30 pop. days. Mean ICU stay was 1±0.4 days; length hospital stay was 3±1 days. No postoperative deaths were observed.

Conclusions: LD liver transplantation remains as a complex procedure, but the evolving experience, the sustained deficit of cadaveric organs, together with an acceptable mortality, increases the team willingness to consider its use, in order to reduce the mortality in the waiting list.
New Index for Prediction of Massive Blood Transfusion

Blanca Otero Torrón1, Clara Fernández1, Alberto A. Marcacuzco1, Lucía Alcoba2, Paula Alvarez2, Silvia Fernández1, María Orellana1, Félix Cambra1, Oscar Caso1, Alejandro Manrique1, Jorge Calvo1, Álvaro Gª-Sesma1, Carmelo Loínez1, Carlos Jiménez1, Iago Justo1.

1General and Digestive Surgery, University Hospital 12 de Octubre, Madrid, Spain; 2General and Digestive Surgery, Faculty of Medicine - Complutense University of Madrid, Madrid, Spain.

Introduction: Massive blood transfusion is a frequent condition amongst liver transplant recipients. Recipient-related risk factors, including cirrhosis, multiple surgeries, and suboptimal donors, can be decreased but not eliminated. The first index designed to predict massive blood transfusion was the McCluskey index, and several more complex mathematical models have followed, without a significant increase in sensitivity. Furthermore, all of these models have failed to include donor characteristics.

Methods: One thousand four hundred and sixty-nine liver transplants were performed at our institution between May 1998 and December 2019, and data was available regarding transfusion for 1469 of them. We divided the patients into two groups, with regards to transfusion of 6 or more units of packed red blood cells in the first 24 hours post transplant, and we analyzed the differences between the groups. We created dichotomic variables in relation to the group median for massive transfusion. Later on, we performed binary logistic regression, we analyzed the risk factors for massive transfusion and created a new index taking into account the results from our multivariable study, assigning one or two points to the most significant variables, using an OR of 1.9 as a cut-off.

Results: Out of the 1198 patients, 607 (50.7%) met criteria for massive transfusion. Both groups were statistically different with regards to hepatocellular carcinoma, autoimmune cause, liver/kidney transplant, uDCD, retransplantation, albumin serum levels, creatinine, sodium, bilirubin, haemoglobin, platelets, INR, MELD, McCluskey and Child scores. Logistical regression analysis of our variables yielded the following results for a new model, including Creatinine (OR 1.97), sodium (OR 1.73), Hemoglobin (OR 1.99), platelets (OR 1.37), INR (OR 1.4), uDCD (OR 2.13) and split liver donation. Upon comparing the different available models, our model presented an AUC of 0.758, which is superior to either MELD, McCluskey or Child scores.

Conclusion: We have created a new prognostic index starting on the most frequently studied variables associated with massive transfusion, and incorporated donor variables for the first time. This new index provides an easy and straight-forward way to assess the preoperative risk of massive blood transfusion for liver transplant.
Decreasing Therapeutic Anticoagulation and Bleeding in Post-operative Liver Transplant Patients: A Single Institution’s Analysis of a Prospective Anticoagulation Algorithm

1Department of General Surgery, University of Utah Hospital, Salt Lake City, UT, United States; 2Transplant Service, Intermountain Medical Center, Murray, UT, United States; 3Hepatology Service, Intermountain Medical Center, Murray, UT, United States; 4Thrombosis Clinic, Intermountain Medical Center, Murray, UT, United States; 5Department of Internal Medicine, University of Utah School of Medicine, Salt Lake City, UT, United States.

Introduction: The incidence of venous thromboembolism (VTE) in patients after liver transplantation (LT) is 0.4% to 15.5%. Management in the acute post-operative setting is challenging given the increased risk of bleeding. The aim of this study was to evaluate the implementation of a standardized VTE risk stratification algorithm to safely decrease the unnecessary implementation of therapeutic anticoagulation.

Methods: 87 (January 2016 - December 2017) and 182 LT patients (January 2018 - March 2021) were enrolled before and after the implementation of the algorithm, respectively. Primary endpoints included therapeutic anticoagulation for the treatment of a VTE within 14 days after LT and clinically significant bleeding. Safety outcomes included return to the operating room for bleeding, readmission, pulmonary embolism (PE), or death within 30 days after LT.

Results: Demographics were similar between groups. Following LT, 23 and 10 patients developed a VTE in the study and control groups, respectively. MELD score (OR = 1.06, 95% CI: 1.01-1.11; p=0.01) and number of operative lines (OR = 1.35, 95% CI: 1.03-1.78; p=0.033) were associated with VTE development. Length of stay was longer among patients who developed a VTE (14 vs 10 days, p<0.001). The study group had decreased odds of receiving immediate anticoagulation, readmission, pulmonary embolism (PE), or death within 30 days after LT.

Conclusions: This risk stratified VTE treatment algorithm in LT patients safely decreased rates of post-operative therapeutic anticoagulation and of clinically significant bleeding without an increase in early adverse outcomes.
Surgical Site Infection in Liver Transplant Patients: Evidence From Real-World Studies

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Objectives: Surgical site infection (SSI) is a common and postoperative complication in patients who underwent solid organ transplant and it makes extensive healthcare burden. So far, the pooled prevalence and microorganisms causing SSI among liver transplantation has not been reported well. This evidence based systematic literature review and meta-analytic approach aimed to find the pooled prevalence of SSI.

Methods: A systematic literature search on PubMed/Medline, Embase was conducted to identify the study determining the prevalence of SSI among patients who underwent liver transplantation. We calculated pooled prevalence (%) with 95% confidence interval (CI) with random-effect model. A meta-analysis was performed using “meta” package through R 3.5.0. software.

Results: A total of 16 studies with 6,012 studied patients were included in this analysis. The rate of SSI was ranged between 9.0% and 96.4%. The pooled prevalence of SSI was 28.52% (95% CI: 17.19 to 41.01%) with high degree of heterogeneity (I² = 99%, heterogeneity-p <0.01). The included studies reported higher percentage of organ-space SSI (70.2%), followed by incisional, superficial and deep SSI. The incidence rate of SSI was ranged from 0.34-10.3 episodes per 100 transplantation. Staphylococcus aureus (76.5%) was the most common pathogen identified, followed by Coagulase-negative staphylococci (35.0%), Escherichia coli (21.25%), Enterococcus faecium and Staphylococcus epidermidis (12.5%), and Candida albicans (6.25%).

Conclusions: The current result suggests the overall prevalence of SSI infection was noted high. However, due to high degree of heterogeneity, resulting considerable amount of clinical uncertainty regarding the prevalence of SSI among patients underwent liver transplantation. Therefore, studies are required to confirm the present findings.

Single Center Study on Liver Transplantation Since 1988: Expected Life Expectancy and Affecting Factors

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Introduction: The purpose of this research paper is to determine the expected life expectancy of liver transplant patients and the factors affecting it.

Materials and Methods: Data of 652 patients who had undergone liver transplantation in the period between December 8, 1988 and December 31, 2021 were analyzed within retrospective cohort study. Surgeries performed by Baskent University team eliminated one of the key factors that would affect the patients’ expected life expectancy in all cases. Dependent variables of the study were defined as cadaveric donor and live donor, whereas the independent variables were defined as age, gender and blood group of donor and recipient, degree of kinship with donor, cancer or other diseases and post-operative complications. The data were uploaded to SPSS and applied the Kaplan-Meier, Cox Regression, T-student and Chi-squared tests.

Results: Average life expectancy in cases with a cadaveric donor is 5151 days (14 years), whereas average life expectancy in cases with a live donor is 6268 days (17 years), meaning that there is a statistically significant difference between the two average life expectancies. By gender of recipients is 5,239 days (14 years) for males and 7,459 days (20 years) for females, meaning that there is a statistically significant between the two average life expectancies. The survival distribution in cases where the donor is a parent of the recipient is 7525 days (20 years), whereas 4170 days (11 years) in case of a sibling donor and 3201 days (8 years) in case of other degrees of kinship. When examined by blood group, Rh factors of all recipient groups and donor groups there is no statistically significant between their survival distributions. When examined by blood group, Rh factors of all recipient groups and donor groups there is no statistically significant between their survival distributions of recipients with cancer and those without. When the recipients’ complications distributions are examined, there is a statistically significant between the survival distributions of cases that suffer a perforation or biliary dilatation.

Conclusion: This study revealed that the donor being a cadaveric or live donor, gender of the recipient, their degree of kinship to the donor, post-operative complications had a statistically significant effect on the expected life expectancy of liver transplant patients, while the fact that there is no significant difference between the survival distributions in cases where the donor is cadaveric or a sibling or another degree of kinship makes the practice of sibling donors questionable.
An Alternative Abdominal Closure Technique After Pediatric Liver Transplant: Bogota-Bag Technique

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Introduction: In conditions such as large for size, postreperfusion hepatic edema, and intestinal edema, primary closure of the abdominal wall can cause respiratory complications, thrombosis of vascular structures due to compression of graft vascular structures, ischemia of the graft, and intestinal complications. In this study, we aimed to compare the results of primary abdominal closure (PAC) and temporary patch closure (bogoto-bag technique) (BB) in pediatric liver transplant recipients.

Material and Methods: The first liver transplant in 1988 was performed by our team. Between 8 December 1988 and 31 December 2021, we performed 701 liver transplant. Of these liver transplants 334 were pediatric and 367 were adults. We performed PAC in 295 recipients. In 39 pediatric liver transplant recipients, we preferred BB technique as the abdominal closure technique in patients with suspected intra-operative tense abdominal closure or intra-abdominal hypertension. In these patients we used this technique, we sutured the sterilized saline bag to the skin at the edge of the defect continuously with a 3/0 polypropylene suture by shaping the defect so as not to cause abdominal hypertension. PAC was achieved in patients after control laparotomies at 48-hour intervals.

Results: The mean age of the PAC group was 8.38 years, while the mean age of the BB group was 2 years. The average weight of the PAC group was 26.38 kg, and the average weight of the BB group was 7.93 kg. Biliary atresia was the most common indication in both groups. In 39 pediatric liver transplant recipients, we preferred BB technique as the abdominal closure technique in patients with suspected intra-operative tense abdominal closure or intra-abdominal hypertension. In these patients we used this technique, we sutured the sterilized saline bag to the skin at the edge of the defect continuously with a 3/0 polypropylene suture by shaping the defect so as not to cause abdominal hypertension. PAC was achieved in patients after control laparotomies at 48-hour intervals.

Conclusion: Temporary patch closure technique can be used safely in experienced centers in low weight and young children, large for size and increased intra-abdominal pressure.

Stereotactic Ablative Body Radiotherapy as a Bridge to Liver Transplantation for Hepatocellular Carcinoma: Başkent University Experience

Güler Yavas1, Ebru H. Ayvazoglu Soy2, Mehmet Coskun3, Cem Onal1, Fatih Boyvat4, Mehmet Haberal1.
1Department of Radiation Oncology, Baskent University, Ankara, Turkey; 2Department of General Surgery, Division of Transplantation, Baskent University, Ankara, Turkey; 3Department of Radiology, Baskent University, Ankara, Turkey; 4Department of Radiology, Division of Interventional Radiology, Baskent University, Ankara, Turkey.

Aim: Hepatocellular carcinoma (HCC) is the most common primary liver tumor. The only curative treatment options remain to be liver transplantation and resection. However approximately 20–30% of the patients have substantial disease progression while still awaiting transplantation. Herein, we report our experience on stereotactic ablative body radiotherapy (SABR) as a bridge to liver transplantation for HCC.

Methods and Materials: We retrospectively evaluated 63 pathologically proven HCC patients who received liver-directed therapy (38 resection, 38 TACE, 27 RFA) while waiting for liver transplant with a mean 74,081 ± 8,732 months of disease free survival. SABR was applied to nine lesions (total diameter ≤6 cm and at least 1 cm away from GIS mucosa or chest wall) in seven Child B HCC patients (with Karnofsky Performance Status ≥70 and no extrahepatic metastases) as a bridge treatment to transplantation. Radiographic response was based on magnetic resonance imaging evaluation at one month after SABR. All patients were assessed evaluated throughout the course of SABR, one month after completion, and at 3-month intervals for the first two years following SABR.

Results: The median age of SABR patients was 65 years (range: 63-71 years) and the median SBRT dose was 45 Gy (range: 30-54 Gy) delivered in 3-5 fractions. The median tumor diameter was 17 mm (range: 12-30 mm). All patients received liver-directed therapies prior to SABR. The median follow-up period was 10 months (range, 2-16 months). Six lesions (66.7%) had a complete response, and 3 patients are still alive with no evidence of disease. The acute toxicity was negligible and all patients completed the course as planned.

Conclusion: Our results suggested that SABR is a feasible, effective and safe bridging therapy option for HCC patients while waiting for liver transplant.
Manangement of Post Liver Transplantation-Tacrolimus Induced Toxicity With Normal Serum Levels

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Introduction: Drug induced liver injury post liver transplantation occurs in 1.7% of the patients. Tacrolimus being an effective immunosuppressant is used to treat acute rejection. However, it rarely can cause toxicity which is demonstrated by cholestatic liver injury. We hereby present the case of a young male, who was a diagnosed case of Wilson’s disease, on pencillamine chelating therapy and underwent living related liver transplantation.

Case: Within a month post transplantation he developed deranged, predominantly cholestatic pattern liver function tests. Laboratory parameters showed Total bilirubin 1.12mg/dl, ALT 553 IU/L, Gamma-glutamyl transferase 624 IU/L and Tacrolimus level of 10.2ng/ml. After thorough evaluation liver biopsy was performed. Liver biopsy documented hepatocellular necrosis with centrilobular cholestasis without any evidence of graft rejection. Although with normal level of Tacrolimus, biopsy was suggestive of drug induced liver injury. Thus, Tacrolimus dose was reduced, which resulted in improvement of his LFTs and was later discharged.

Conclusion/ Discussion: We have demonstrated tacrolimus induced toxicity in liver transplant recipients, despite normal serum levels. Thus, transplant physicians should keep high index of suspicion regarding toxicity in post-transplant setting. Tacrolimus is an effective post liver transplantation immunosuppressant and has the ability to treat early acute rejection. Liver biopsy documented hepatocellular necrosis with centrlobular cholestasis without any evidence of graft rejection. Cholestatic liver injury after tacrolimus usually resolves after dose reduction or by switching to another agent.

Different Severity and Disparate Clinical Outcomes Between EAD Sub-Criteria and Proposal of a New EAD Classification After Liver Transplantation

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Background: The current binary definition of early allograft dysfunction (EAD) is not sufficiently accurate for discriminating clinical outcomes after liver transplantation (LT). It is also criticized for including heterogeneous diagnostic criteria with disparate severities of clinical outcomes. We investigated whether there are significant differences in clinical outcomes among three EAD sub-criteria and explore the necessity of dividing EAD into different stages like acute kidney injury to grade the severity of graft dysfunction.

Methods: A total of 707 consecutive LT patients from 2015 to 2020 were retrospectively reviewed. EAD patients were divided into 3 subgroups based on different sub-criteria: i) EAD-type-A: only elevated AST/ALT >2000 U/L within postoperative day 7 (POD 7); ii) EAD-type-B: bilirubin ≥10 mg/dL or INR >1.6 on POD 7; iii) EAD-type-C, meeting two or three of the bilirubin, INR and ALT/AST criteria. Peri-operative clinical complications and survival outcomes were compared between these subgroups.

Results: Three-month graft failure in non-EAD, EAD-type-A, EAD-type-B and EAD-type-C were 1.6%, 3.5%, 12.8% and 29.6%; One-year patient survival was 94.6%, 93.6%, 81.3% and 71.2%, respectively. EAD-type-B and EAD-type-C were significantly associated with longer hospital stay, ICU stay, ventilator support time, higher rates of AKI, RRT, in-hospital death, and inferior one-year survival outcomes (P<0.001); However, there were no statistical differences between non-EAD and EAD type A(P>0.05). A new EAD classification with three stages was reclassified to grade the severity of post-LT graft dysfunction. In ROC analysis, new EAD classification had an excellent overall AUROC of 0.84(0.81-0.86) in determining 3-month graft failure, superior to the binary EAD (AUROC=0.73, CI 0.70-0.77, P<0.001) and MEAF for Early Allograft Function Scoring(MEAF) (AUROC=0.76, CI 0.73-0.79, P<0.001), similar to the Liver Graft Assessment Following Transplantation score(L-GrAFT-7) (AUROC=0.87, CI =0.84-0.90, P<0.05).

Conclusions: Different EAD sub-criteria experiences significantly different clinical outcomes. The binary EAD definition could be further reclassified into several sub-stages with different severity. The new EAD with 3 stages could serve as an effective tool to simply stratify the severity of graft dysfunction after LT.
Low Intra-Operative Urine Output Is Associated with the Development of Severe Acute Kidney Injury And Continuous Renal Replacement Therapy Requiring After Liver Transplantation

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Acute kidney injury (AKI) is associated with adverse outcomes after liver transplantation(LT). The impact of intraoperative urine output(UO) on post-LT AKI remains unclear. 660 consecutive LT patients between 01/2015–12/2020 were analyzed. The rates of non-AKI, AKI-I, severe AKI(AKI-II and -III) were 51.5%, 22.7% and 25.8%, 38.1% and 89.1% AKI cases were developed during operation or within 72h after LT. As AKI severity rose, the proportion of SAKI patients remarkably increased from 19.3% to 65.7% and creatinine maintained at significantly higher levels within one year. SAKI patients had inferior 90-day, 1- and 3-year survival compared with non-AKI and AKI-I patients (p<0.001). Low UO was independently associated with AKI and continuous renal replacement therapy(p<0.001), with best cut-off of 1.84ml/kg/h(AUC 0.780) and 1.38 ml/kg/h(AUC 0.838). Low UO(<1.84ml/kg/h) was an independent risk factor for major adverse kidney events(OR 2.262, p<0.001), 90-day mortality(HR 3.795, p<0.001), and one-year mortality(HR 2.877, p<0.001). Patients experiencing both low UO and AKI had the worst 3-year patient survival compared with those having either low UO or AKI( p<0.001). In conclusion, SAKI was mainly developed in operation. Intraoperative UO was a strong predictor for SAKI and should be carefully monitored to guide patient management and early intervention for renal dysfunction.

Respiratory syncytial virus Pneumonia in a LDLT Recipient Transplanted for COVID 19 Precipitated ACLF: Managed With Ribavirin and IVlg

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Introduction: Respiratory Syncytial virus causes severe illness in children and immunocompromised elderly persons on chemotherapy but has been reported rarely in liver transplant recipients. we report a case of a living donor transplant recipient who presented with severe RSV pneumonitis following urgent LDLT for ACLF.

Method: 63 yr NASH cirrhosis with DM type I, prior CABG 10 yrs ago was initially listed at MELD 15 for DDLT. He was infected with COVID 19 during the second wave of infections in India requiring hospitalisation, developed ACLF grade 1 with SBP, AKI and HE; advised early LDLT. A suitable related ABO compatible donor was found and evaluated. pre op Covid PCR was negative both donor and recipient. Pre Transplant MELD Na was 31.

Result: Right lobe LDLT (with Spleenic artery ligation was performed. The graft weighed 630 gm(GRWR 0.84). Due to high intraop portal flow (310ml/100gm/min) SAL was done with final flow 210ml/100gm/min. Received Basiliximab 20mg intraop and D4 and Steroid 10 mg per kg that was tapered to 20mg by D5, tacrolimus started d4 with target levels 8-12 by D7. Post op course complicated by hypoxicic delirium that gradually improved. Shifted to room on D14. During discharge planning and education developed CMV viremia with thrombocytopenia and anemia. Managed with oral therapeutic Valganciclovir for 2 weeks then prophylactic dose continued. D22 worsening cough and febrile illness. Antibiotics and antifungals restarted. CMV DNA PCR and all cultures were negative. Developed worsening chest infiltrates and hypoxemia requiring intubated and ventilation. Serum and BAL for galactomannan, Beta glucan and Pneumocystis staining were negative. PCR based respiratory virus panel positive for RSV. Started on IVlg (0.4 gm/kg x 4 days) &Rivabivir (15mg/kg, 4 weeks). Tracheostomy done on D5 of intubation. Became afebrile after 3 days of therapy with gradual improvement in respiratory parameters and chest imaging. RSV DNA negative after 3 weeks. Finally tracheostomy removed and discharged on D 65.

Conclusion: This patient had multiple predisposing factors for RSV (age, DM, immunosuppression and CMV). Prior COVID 19 pneumonia is likely another factor responsible for developing RSV. Respiratory viral panel including RSV PCR is recommended in elderly Liver Transplant recipients to diagnose atypical pneumonitis not responding to antibiotics and antifungals. Ribavirin and IVlg may help in salvaging these sick patients. RSV vaccine once available should be added to pretransplant protocol in elderly and other high risk recipients.
P9.30
Salvaging Small for Size Grafts With Splenic Artery Embolization in Living Donor Liver Transplant: Older Liver May Not Recover
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Introduction: Small for size (SFS) is a dreaded problem after LDLT. Portal hyperperfusion (large spleen) or outflow issues can cause functional SFS despite adequate GRWR (> 0.8). SAE (Splenic Artery Embolization) reduces portal flow allowing the graft to recover and regenerate. However, despite SAE, older grafts may not recover from the hyperperfusion injury. We report 3 cases which required SAE and discuss the outcomes.

Method: Medical records of 3 male patients with right lobe LDLT (donors - spouses) who underwent SAE with a diagnosis of SFS were reviewed. Median MELD was 25 and donor age were 39, 40 and 59 years. Two were presented with functional SFS; GRWR 0.83 and 0.82 (RIHV thrombosis leading to hyperperfusion); 1 patient (hyperperfusion due to enlarged spleen; GRWR 0.89) also had Splenic arterial steal on Doppler (patent artery on CT angiography). All 3 had initial reduction of bilirubin and INR till POD4 followed by worsening LFT and ascites. SAE was done after Doppler findings/Triphasic Doppler, which showed continuous >30% reduced portal flow and pressure recording may be used to perform Splenic artery ligation or Splenectomy to prevent SFS.

Results: SAE was successful in reducing portal flow in all 3. The patients with younger grafts (Donor age < 45) showed rapid improvement; normalization of bilirubin and disappearance of ascites over next 2 weeks. However, the patient with older graft after showing initial reduction of bilirubin and ascites (Doppler showed continuous >30% reduced portal flow) had worsening jaundice, ascites, coagulopathy and hypoalbuminemia. He subsequently developed severe graft dysfunction and septicaemia and expired.

Conclusion: SFS can manifest despite adequate GRWR (> 0.8), if outflow issues/hyperperfusion are present. SAE works well in salvaging SFS post operatively, but older livers may not have enough reserve to recover. When accepting older livers, intra op flow and pressure recording may be used to perform Splenic artery ligation or Splenectomy to prevent SFS.

Figure 1 Splenic colling enhancing HA flow

P9.31
Devising Bile Duct Anastomosis to Reduce Biliary Complications in Living Donor Liver Transplantation at Our Hospital
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Background: Living donor liver transplantation has become an important treatment for end-stage liver disease. In living donor liver transplantation, the biliary tract is thinner and shorter than in deceased donor liver transplantation. For this reason, it has been reported that biliary complications are more frequent in living donor liver transplantation. We have been devising bile duct anastomosis to reduce bile leak and biliary stricture. In this study, we examined the results of our efforts and report the changes in the surgical technique and perioperative management at our hospital.

Methods: 210 patients who underwent living donor liver transplantation at our hospital by November 2021 were included in this study. Conventionally, biliary tract reconstruction was performed under direct vision with a circumferential interrupted suture and placement of an internal short stent. From March 2013 to May 2016, microsurgical outer knotted suture was used to reconstruct the biliary tract without sutured knots in the lumen. After a period of regression to the conventional method, since May 2019, biliary tract reconstruction has been performed with continuous sutures on the posterior wall and interrupted sutures on the anterior wall and external drainage as the basic stenting technique. 28 patients since May 2019 and 182 patients before May 2019 were divided into two groups. The incidence of bile leak and biliary stricture was examined. Risk factors for bile leak and biliary stricture were also examined in univariate and multivariate analysis.

Results: Among all patients, bile leak was observed in 29 cases and biliary stricture was examined. Risk factors for bile leak and biliary stricture were also examined in univariate and multivariate analysis.

Conclusion: In the present study, biliary tract reconstruction with continuous sutures on the posterior wall and interrupted sutures on the anterior wall and external drainage, which is currently performed at our hospital, showed no significant difference from conventional methods in both bile leak and biliary stricture. Because of the small number of cases, further study is needed in the future.
P9.32
Excellent Outcome Quality Is Not Dependent on a High Caseload in Liver Transplantation
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Background: Today’s dogma without clear evidence is that case volume correlates with patients’ outcome after liver transplantation (LT). Thus, we prospectively analyzed the outcomes in our low volume center, which is characterized with strong interdisciplinary and interprofessional concepts.

Methods: Our LT program was re-organized and re-structured in 2016 including a center-embedded interdisciplinary and interprofessional team concept with new clinical standards for the peri-, intraoperative and follow-up management of patients. In parallel, routine pre-transplant histopathological evaluation of donor organs was established. Outcomes of 166 adult LTs (125 male; median age of 55.4 years [19 to 74 years]) performed between November 2016 and November 2021 was documented in a prospective database driven manner and compared with high volume centers. Kaplan-Meier method was used for long-term patient and graft survival.

Results: 1-/ 5-years patient and graft survival was 95.3%/ 91.8% and 82.7% and 78.4%, respectively. The median ICU stay was 2 days [1-125 days] and the median hospital stay was 15 days [7-187 days]. Hospital readmissions were necessary within the first 30 days and 1 year after discharge in 8% and 16% of cases, respectively.

Conclusion: Clearly defined standards developed within an interdisciplinary and interprofessional team concept result in best possible outcome quality of treatment after LT independent of caseload.

P9.33
Prevention Strategies Against CMV-Infection After Liver Transplantation
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Background: There is a variety of prevention strategies against cytomegalovirus (CMV) viremia/ disease after liver transplantation (LT). Thus, this retrospective cohort study performed in a prospective manner with a 1-year follow-up has been performed comparing anti-CMV immunoglobulins (IGs) with Valganciclovir.

Patients and Methods: A total of 257 patients underwent LT between January 2008 and May 2020. While 134 patients received anti-CMV-IGs (7500 IU for 4 days) between 2008 and October 2016, 111 patients were treated with Valganciclovir (up to 900 mg/d for 3-6 months dependent on renal function and side effects) since November 2016. Patients with viremia in both groups were treated at least for 14 days with Ganciclovir or Valganciclovir. Primary endpoint of the study was CMV viremia within 1 year after LT. Secondary endpoints were leukopenia, renal function, patient and graft survival.

Results: Demographics were comparable in both groups (i.e. age (56.6 +/- 11.2 years), gender (78.8% male)). Viremia was 36.7% (n=90) within 1 year after LT with 43.3% (n=58) after anti-CMV IGs vs. 28.8% (n=32) after Valganciclovir (p>0.05). The incidence of viremia was dependent of the donor-recipient match with 39.6% (n=21) and 60.6% (n=20) in D-/R+ and D+/R+ after anti-CMV IGs, and 12.0% (n=3) and 25.7% (n=9) after Valganciclovir (p=0.018; p=0.007), respectively. The overall 1-year mortality rate was comparable in both groups with 13.1% (n=32). Kidney function based on serum creatinine was significantly improved with anti-CMV IGs at 1 year after LT.

Conclusion: While Valganciclovir protected nicely CMV positive recipients from CMV viremia the effect of anti-CMV IGs was inferior in this constellation without any impact on CMV disease; however, anti-CMV IGs are in favor to a better side effect profile especially concerning renal function and thus it should be the preferred prevention strategy.
Application of Mesenchymal Stem Cells for the Treatment of Liver Graft Dysfunction Caused by Chronic Rejection. Case Report

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Background: Development of immunosuppressive therapy (IST) complications after liver transplantation (LT) requires its minimization. Decrease of immunosuppression in the long-term period after transplantation in 8% of patients is accompanied with the development of chronic rejection (CR).

Objective: The aim of this report was to demonstrate the successful treatment of liver transplant CR with mesenchymal stem cells (MSCs) in patient with acute kidney injury (AKI) and IST minimizing.

Results: Patient with unresectable liver alveococcosis underwent LT. After surgery patient received a three-component IST, which after six months was de-escalated to tacrolimus monotherapy (Tac). A year after the operation graft dysfunction developed, which was accompanied by a maximum increase of AST up to 511 U/l and ALT up to 507 U/l, GGTP up to 1753 U/l and ALP up to 474 U/l. IST was escalated: pulse therapy with glucocorticosteroiids was performed twice; mycophenolate mofetil, mTOR inhibitors, intravenous immunoglobulin were added. Thrice performed puncture liver biopsy demonstrated the chronicity of the alloimmune conflict. Developed AKI in the process of anti-rejection therapy required decreasing of Tac, which led to increase of cytolyis and cholestasis. Infusion of allogeneic MSCs with a total dose of 8 x 10^6 cells per kg led to normalization of laboratory blood tests. The Tac concentration was 0.8 ng/ml; kidney function recovered: urea level was 7.1 mmol/l, creatinine - 80 µmol/l, GFR - 25 ml/min. Application of MSCs formed immunotolerance: the suppressor subpopulation of T-regulatory CD3+CD4+CD25highCD127- lymphocytes increased and effector CD3+CD8+ naïve T-lymphocytes, antigen-presenting myeloid dendritic cells, and antibodies-producing CD19+ naïve B-lymphocytes decreased.

Conclusions: MSCs can be used in CR as an effective alternative IST that can replace the immunosuppressive effect of basic immunosuppressants.

Application of CRL-Classification (J. Yan ET AL., 2020) Principles for Description of Rare Hepatic Artery Anomalies

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Background: Nowadays publications dedicated to the anatomy of the hepatic artery (HA) continue to be published and associated with rather high its variability.

Objective: The aim of the study was to establish the variants of HA; apply morden principles for description of rare HA anomalies.

Materials: Study included a retrospective analysis of CT-angiography data of 60 patients. Variants of the anatomy of the hepatic arteries were classified according to the proposed in 2020 by J. Yan et al. hepatic artery anatomy classification based on the three-dimensional CT. This classification is based on such parameters as the type of the aberration and the place of origin for the three main hepatic arteries: common hepatic artery (CHA) – «C», right hepatic artery (RHA) – «R» and left hepatic artery (LHA) – «L». In this case, the first letter indicates the described vessel (C, R, L), the second letter - the nature of the aberration (a - additional, r - replaced), the third letter - the place of origin (A - aorta, C – truncus celiacus, G - gastroduodenal artery (GDA), L – left gastric artery (LGA), S – superior mesenteric artery (SMA), O - other).

Results: Normal HA anatomy was observed in 41 patients (68.3%). Anomalies of the LHA were observed in 6 (10.0%) patients. At the same time, the LHA arose from the LGA: accessory LHA (CRLa) – 4, replaced LHA (CRLr) – 2. Anomalies of the RHA with origin from the SMA and GDA were observed in 3 (5.0%) patients: replaced RHA from the SMA (CRrSL) was noted in 1 patient, an additional RHA from the GDA (CRaGL) – in 2 patients. Simultaneous atypical arising of the left and right HA was noted in 5 (8.3%) patients. LHA arose from the LGA, RHA from the SMA in 3 cases (CRrL). The RHA from the GDA in 2 cases (CRrL). Separate arising of the CHA from the SMA (CRL) or LGA (CRL) was not revealed, its anomalous origin was combined with anomalous arising of the other hepatic arteries. Such combined variants were revealed by us as rare and were observed in 5 cases (8.3%).

To unify the rare variants with the CRL classification, we proposed to use the same letter designations for the “non-hepatic” arteries, separating them from the “hepatic” ones with square brackets, for example: [CRL]LA - classical anatomy of the CHA, RHA, LHA + LGA from aorta; [CRL]LA - CHA from SMA + LGA.

Conclusions: 1) Anomalies of the HA occur frequently: almost third of patients (31.7%) had abnormal variant of HA, while a combination of several anomalies (16.7%) is possible; 2) proposed classification is convenient for protocoling anomalies of the HA; 3) application of the proposed CRL-classification allows exactly indicate the peculiarity of rare and combined anomalies of the HA, as well as take into account the peculiarity of non-hepatic arteries that vascularize organs of hepatopancreaticobiliary area.

Abstracts
**P9.36**

**Impact and Consequences of Recipient Gastroduodenal Artery (GDA) Ligation Prior to Hepatic Artery (HA) Anastomosis During Orthotopic Liver Transplantation (OLT)**

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**Background:** The recipient GDA is often ligated before the HA anastomosis during OLT either to gain mobility, length on recipient HA and with hypothesis that it would prevent “Steal syndrome” protecting the anastomosis. The aim of study is to evaluate its impact on prevention of HA thrombosis (HAT) and consequences of such ligation.

**Methods:** A retrospective analysis of cadaveric OLT (n=210) with recipient GDA ligated (Group 1) or not (Group 2). Impact was evaluated by occurrence of HAT and consequences by post-operative hyperamylasemia (POHA), nausea and vomiting and delayed feeding.

**Results:** Group 1 included 78 (37%) cases where common HA was used for anastomosis, Group 2 had 132 (63%) cases where right HA or the proper HA was used for anastomosis Table 1.

There was no incidence of hepatic artery thrombosis (HAT) reported in either group. In Group 1, 31 out of 78 (39.7%) patients were reported to have post-operative hyperamylasemia (POHA) ranging between 200 and 4700 Units/liter accompanied by delayed feeding, whereas in Group 2, 16 out of 132 (12%) patients had POHA ranging between 200-1400 Units/liter (p value of <0.01 using Fisher’s exact test).

**Conclusions:** Ligation of recipient GDA is not associated with decreased risk of HAT as compared to non-ligation. However, it does have consequences in the form of possible POHA leading to delayed feeding due to decreased oral tolerance.

<table>
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<th>Group 2</th>
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<td>24 (11.9)</td>
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<td>12 (9.1)</td>
<td>24 (11.5)</td>
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<td>Replaced esophagus/bronchus, n(%)</td>
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<td>17 (12.9)</td>
<td>21 (10.5)</td>
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<td>Delayed feeding, n(%)</td>
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<td>9 (6.8)</td>
<td>42 (20.0)</td>
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**P9.37**

**Liver Transplantation for Abernathy Malformation (Congenital Absence of Portal Vein): A Case Report**

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**Introduction:** Congenital absence of portal vein (CAPV) is very rare congenital anomaly caused by dysplasia in the portal vein (PV) system leading to diversion of blood from gut directly to IVC without passing liver. Clinically after being asymptomatic it can present with encephalopathy from hyperammonemia and hypoglycemia.

**Case report:** A 8-year old female child who was diagnosed with CAPV was referred to our centre for further evaluation. She was a full-term baby and doing well till 4 years of age when she had near fainting. During evaluation she had elevated liver function test, splenomegaly and imaging revealed CAPV with shunting. Her family reported decline in her academic performance over past few years. On index visit her total bilirubin was 1.4 mg/dL, AST 40 IU/L, ALT 29 IU/L and serum ammonia 122 ug/dL with no evidence of hepatopulmonary syndrome. The CECT abdomen revealed common trunk of splenic vein and SMV, directly draining into IVC with prominent hepatic artery (Figure 1). She received deceased donor liver transplant from brain dead donor (Figure 2) and postoperative course was uneventful. Liver function has remained stable with patent PV and hepatic artery. Histology of the native liver showed absent PV with nodular liver parenchyma without cirrhosis.

**Discussion:** CAPV can lead to encephalopathy and mental retardation; hence careful observation of their symptoms, hepatic function, and metabolic abnormalities is required. LT might be indicated for symptomatic CAPV or prophylactic LT is indicated before the development of pulmonary hypertension or HPS.
Long-term Outcome of Liver Transplantation Versus Resection For Hepatocellular Carcinoma: A Single-Center Experience

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Introduction: Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer deaths worldwide and typically has a poor prognosis. Liver transplantation (LT) and liver resection (LR) are the mainstay treatments for HCC. We compared the clinicopathologic features and long-term prognosis between patients receiving LT and LR for HCC.

Methods: All patients who underwent LT or LR from 2010 to 2020 for HCC at Hume-Lee transplant center were included. A total of 321 patients (137 LR, 184 LT) were enrolled. Overall survival (OS) and disease-free survival (DFS) were investigated and compared between LT and LR according to the Milan criteria. Univariate and multivariable analyses including clinicopathologic factors were performed for both groups.

Results: There were significant differences in clinicopathologic factors between LT and LR groups: male sex (83.2%, 69.3%; p = 0.004), race (Caucasian 73.4%, 43.8%; p<0.001), MELD (mean 17.1, 8.74; p<0.001), cirrhosis (92.8%, 71.8%; p <0.001), microvascular invasion (24.4%, 54.8%; p <0.001), within Milan criteria (75.0%, 41.6%;p <0.001). The overall survival rates at 1, 5, and 7 years for LT and LR groups were 94.0%, 77.5%, 71.1% vs 79.3%, 48.3%, 38.5%, respectively (p <0.001). The disease-free survival rates at 1, 5, 7 years were 98.2%, 84.6%, 84.6% vs. 71.9%, 42.5%, 24.8%, respectively (p <0.001). Patients within Milan criteria showed no significant difference in the overall survival rate at 1, 5, and 7 years between LT and LR (93.3%, 80.4%, 76.3% vs. 92.7%, 69.3%, 52.0%; p=0.17). However, for patients beyond the Milan criteria, LT group showed significantly better overall survival rate compared to LR group (p=0.002). Regarding disease-free survival rates, LT groups showed significantly better survival compared to LR both within and beyond Milan criteria (p <0.001). In multivariable analysis, Milan criteria was the only significant prognostic factors for disease-free survival in both groups (HR 31.29, 95% CI 1.19-818.06 in LT, p=0.039; HR 4.516, 95% CI 1.27-16.04 in LR, p=0.020).

Conclusions: Liver transplantation is associated with better long-term clinical outcomes than liver resection for the treatment of HCC.
P9.39

Long-term Outcome of Open Versus Minimally Invasive Hepatectomy for Hepatocellular Carcinoma: A Single-Center Experience

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Introduction: Hepatocellular carcinoma (HCC) is the fourth leading cause of cancer deaths worldwide and typically has a poor prognosis. Surgical resection is still regarded as the first choice of treatment for HCC. With advances in technology and techniques for liver resection, minimally invasive surgery has now become the standard of care in almost all fields of general surgery, including hepatectomy. We compared the clinicopathologic features and long-term prognosis of HCC between open hepatectomy (OH) and minimally invasive hepatectomy (MIH).

Methods: All patients who underwent OH and MIH from 2010 to 2020 for HCC at Hume-Lee transplant center were included. A total of 134 patients (108 OH and 26 MIH) were enrolled. Clinicopathologic features were compared between two groups under retrospective data analysis. Overall survival (OS) and disease-survival survival (DFS) were investigated and compared between two groups.

Results: Among 26 cases of MIH, 13 patients underwent robotic surgery, and 13 patients underwent laparoscopic surgery. There were significant differences in clinicopathologic factors between OH and MIH groups: age (mean 60.1 years old, 66.9 years old; p = 0.015), resection extent (major hepatectomy 56.5%, 7.7%; p <0.001), operation time (337 min, 267 min; p = 0.013), transfused volume (268ml, 107ml; p = 0.048), tumor number (1.8 [SD 1.24], 1.04 [SD 0.45]; p<0.001), and length of hospital stay (mean 8.7 days [SD 6.7], 5.69 days [SD 2.9]; p <0.010). However, there were no statistically significant differences in tumor size, microvascular invasion, macrovascular invasion, cirrhosis, and ratio of R0 resection. The overall survival rates at 1, 3, and 5 years between OH and MIH groups were 79.3%, 62.4%, 47.9% vs. 79.7%, 52.9%, 44.1%, respectively (p = 0.484). The disease-free survival rates at 1, 3, and 5 years between two groups were 75.0%, 43.0%, 40.0% vs. 73.2%, 53.4%, 40.0%, respectively (p = 0.729).

Conclusions: Minimally invasive surgery for HCC showed a fast recovery and similar oncologic long-term outcome compared to open hepatectomy.

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P9.40

Liver Transplantation for Secondary Hemophagocytic Lymphohistiocytosis Associated Acute Liver Failure: A Case Report

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening syndrome characterized by pathologic macrophage activation. Clinical features include fever, cytopenia, hepatosplenomegaly, and coagulopathy. Liver dysfunction is often seen in HLH patients and occasionally leads to acute liver failure (ALF). There is limited data using liver transplantation (LT) to treat HLH associated ALF (HLH-ALF).

Methods: We present a pediatric HLH-ALF case treated with living donor liver transplantation from her mother and summarize the diagnosis and treatment.

Results: A 4-year-old girl was admitted to the hospital with intermittent fever for more than two months. Although the patient was diagnosed with idiopathic thrombocytopenic purpura two years ago, work-up for infectious and autoimmune causes was negative. Differential diagnosis of lymphoma was considered but was eventually ruled out by lymph node biopsy. After antibiotic treatment, the patient’s temperature dropped to normal, and was discharged. The patient had repeated illness outside the hospital and presented for recurrent high fever(40℃) with hepatosplenomegaly and coagulopathy. The Symptomatic treatment was ineffective; the patient deteriorated rapidly with highly elevated transaminases and serum bilirubin, cytopenias, highly elevated ferritin and sCD25, Bone marrow biopsy revealed foamy macrophages engulfing mature and precursor erythrocytes, consistent with HLH. The patient’s total bilirubin was continually increased and diagnosed secondary HLH-ALF, PELD score 38. The patient was referred to our center for preparing liver transplantation. Considering the patient’s critical condition, she received living donor liver transplantation from her mother (left lobe). The patient recovered well, the liver function improved and the jaundice gradually disappeared after liver transplantation.

Conclusion: The experience described here demonstrates the effect of LT in the treatment of HLH-ALF. Early investigation and treatment should be taken in HLH patients presenting with ALF. However, if liver dysfunction progresses rapidly, LT combined with posttransplant HLH-directed therapy offers the potential for improved survival.
**P9.41**

**Outcomes of Live Donor Liver Transplantation in Adult Patients With HPS – 10-Year Experience From a Single Centre: A Retrospective Analysis**

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**Introduction:** Hepatopulmonary syndrome (HPS) is characterised by hypoxia and is associated with a worse prognosis in patients with cirrhosis. Liver transplantation is the only definitive treatment. We report our 10 year experience of live donor liver transplant in adult patients with HPS.

**Methods:** Seventeen patients with HPS (age ≥ 18 years) and cirrhosis who underwent LDLT during the period 2012 – 2022 were retrospectively analysed. HPS was defined as PaO2 < 80 mmHg in presence of demonstrable macro-aggregated albumin (MAA) scan shunt fraction >6%.

**Results:** The study group composed of 15 male and 2 female patients, mean age 51.05 ± 7.67 years. The most common presentations was dyspnoea, seen in 82.35% patients followed by ascites (76.47%) and gastrointestinal bleed (41.18%). Mean Child Pugh score was 10.52 ± 1.77, model for end-stage liver disease (MELD) score was 20.35 ± 7.38. One patient had very severe HPS (PaO2 <50 mmHg), four had severe HPS (PaO2 50 - 60 mmHg) and twelve had moderate HPS (PaO2 60 - 80 mmHg). The mean MAA shunt fraction was 24.05 ± 18.52% and mean PaO2 was 66.77 ± 10.63 mmHg. All patients underwent right lobe LDLT. The overall time to extubation was 1.23 ± 0.83 days and for ICU stay8.66 ± 0.55 days. Patients received oxygen for a median of 3 [2 – 5] days post-transplant. The main complications in post-LT course were sepsis and neurological, both seen in 3 patients each (17.64%). Overall survival at a median follow up of 54.5 [17 – 76] months was 82.35%.

**Conclusion:** LDLT in HPS is feasible and is associated with good outcomes.

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**P9.42**

**Ventral Hernia Repair Following Liver Transplantation: Outcome of Repair Techniques and Risk Factors For Recurrence**

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**Introduction:** Patients undergoing liver transplantation are at increased risk of developing incisional hernia which can seriously affect their postoperative course and quality of life. This retrospective study identifies pre- and post-operative risk factors for incisional hernia development following liver transplantation.

**Methods:** We conducted a retrospective case-control study on 202 patients undergoing liver transplantation from 2007-2019. 101 selected patients who underwent liver transplantation followed by incisional hernia occurrence were compared with 101 age and date matched controls who did not form a hernia post-transplant. Incisional hernias were repaired open with sublay or retrorectus mesh or by primary closure. Age, sex, body mass index (BMI), transplant indication, pre-operative MELD score, post-transplant complications and immunosuppressive medications were compared between the two groups. Hernia repair outcomes including surgical site infection (SSI), other wound complications, length of hospital stay, and hernia recurrence were analyzed.

**Results:** Patient characteristics between the two groups were well matched. The average time from liver transplantation to incisional hernia occurrence was 20 months. Significant risk factors for incisional hernia occurrence were transplant incision type, specifically midline incisions (0 vs 20 patients, p=0.01). There was a trend toward hernia occurrence with post-transplant take-back laparotomy (12 vs 22 patients, p= 0.06). When analyzing factors associated with recurrence after hernia repair, interestingly viral hepatitis had a significantly lower rate of hernia recurrence (p=0.03). Furthermore, hernia recurrence was impacted by a higher pre-transplant MELD score (score of 16 vs 22, p=0.05), takeback laparotomy post-transplant (17% vs 40%, p=0.03), retrorectus mesh repair of initial hernia repair (18% vs 50%, p=0.01), and post-hernia SSIs (11 vs 32%, p=0.02). No differences were observed for age, sex, BMI, immunosuppressive medications, and hernia defect size.

**Conclusion:** These results highlight important risk factors for hernia occurrence and recurrence post liver transplant including post-transplant takeback laparotomy, hernia repair technique, and SSIs. With regards to the repair technique, intraperitoneal sublay mesh reduces hernia recurrence and is a safe option for incisional hernia repair in this complex patient population.
Conversion Surgery After Radical Chemotherapy Using Living Donor Liver Transplantation for Locally Advanced Unresectable Perihilar Cholangiocarcinoma Without Neoadjuvant Radiation

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Introduction: Because of including crucial blood vessels in portal area, perihilar cholangiocarcinoma (pCCA) is sometimes unresectable. Recently, there have been several reports about those cases prognosis of improving drastically with transplantation and combined chemoradiation therapy. However, liver transplantation for pCCA has some problems. The first is that pCCA is located at a lethal position and its progress is sometimes rapid; therefore, the optimal timing of transplantation is lost. The second is vascular complications associated with neoadjuvant radiation. To overcome these problems, we performed conversion surgery using LDLT with simultaneous resection of the hepatic artery and portal vein, instead of neoadjuvant radiation. Herein, we report our experience of interposition reconstruction.

Methods: The patient is a 31-year-old man with primary sclerosing cholangitis (PSC). He was diagnosed with locally advanced pCCA. His pCCA was unresectable (Bismuth type IV). The patient underwent radical chemotherapy (gemcitabine/cisplatin/S-1) and avoided radiation. After 6 months, his pCCA were well-controlled, except for the local area. However, there was no time to wait brain death donor. Then, we immediately performed LDLT with simultaneous resection of the hepatic artery and portal vein, instead of neoadjuvant radiation. Herein, we report our experience of interposition reconstruction.

Results: The recipient recovered and was discharged 31 days post-transplantation. His liver function improved, and he has no recurrence after LDLT for 6 months.

Conclusion: LDLT with neoadjuvant radiation is associated with high risk of vascular complications. In some cases, conversion surgery after radical chemotherapy using good timing LDLT without radiation may increase chances of transplantation for locally advanced pCCA.

Single-Cell RNA Transcriptomics Reveals Intrahepatic Macrophage Remodeling in Hepatitis B-Related Acute-Onchronic Liver Failure

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Introduction: Acute-on-chronic liver failure (ACLF) is an acutely decompensated cirrhosis syndrome with a high short-term mortality rate. In China, hepatitis B virus (HBV) infection is the main cause of chronic liver disease (CLD). Immune dysregulation is thought to be involved in the progression from CLD to ACLF, which involves systemic inflammation and exacerbation of the innate immune system resulting in multiple organ failures and immunosuppression. Macrophages perform as one of the most important undertakers of hepatic innate immunity, but the understanding of the roles of macrophages in the pathogenesis and immunoregulation of ACLF is limited. Here, we explored the macrophage remodeling during CLD-ACLF process with the single-cell RNA sequencing (scRNA-seq) technology.

Methods: 4738 intrahepatic macrophages from 2 healthy donors (HDs), 5 CLD and 5 ACLF patients as well as 1732 peripheral blood monocytes from 2 ACLF and 1 CLD patients were analyzed by scRNA-seq. Intrahepatic macrophage sub-populations derived from scRNA-seq were confirmed by immunohistochemistry (IHC) and immunofluorescence (IF). Fatty acid (FA) metabonomic was used to qualitative and quantitative analyzed the intrahepatic free FA during ACLF.

Results: ACLF patients exhibited more intrahepatic macrophages than those of CLD patients and HDs. Increase of APOE+TREM2+ anti-inflammatory macrophage subpopulation and exhaustion of SPP1+ M2-like macrophage subpopulation and Kupffer cells (KCs) were the main features of intrahepatic macrophages of ACLF patients. Not the proliferation of the intrahepatic macrophages but the monocyte-derived macrophages (MoMFs) migration into liver was the reason for intrahepatic macrophages expansion in ACLF. Multiple FAs were increased in ACLF liver, which resulted in pro-inflammatory macrophages transformation into anti-inflammatory macrophages and contributed to immunosuppression during ACLF.

Conclusions: During ACLF, KCs were replaced by the MoMFs. Intrahepatic macrophages were transformed from pro-inflammatory states to anti-inflammatory states, which was regulated by increased free FAs in the ACLF liver. TREM2 and intrahepatic FAs may be the potential target for ACLF treatment.
P9.45

**Report of the First Cases of Hepatic SPLIT for Liver Transplantation in Peru**

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**Introduction:** Liver SPLIT is the surgical technique used in liver transplantation in which a liver graft from a cadaveric donor can be used for two recipients on the waiting list, these recipients being both adults and one adult and one pediatric. In Peru, a country with a poor donation rate, the implementation of this technique was very beneficial since through it we expand the donation pool and we can help our patients on the waiting list for liver transplantation.

**Materials and methods:** In the first transplant operation with the SPLIT technique, it was from a 33-year-old donor. Cause of death Ischemic stroke, ideal, who underwent complete right and complete left hepatic partitioning for a 48-year-old adult male diagnosed with autoimmune hepatitis and a 13-year-old female patient diagnosed with cystic fibrosis and hepatopulmonary syndrome. In the second transplant operation with the SPLIT technique, it was from a 37-year-old donor, cause of death due to severe ECT, ideal, who underwent complete right and complete left hepatic partitioning for a 52-year-old adult female patient with cirrhosis due to virus C and a 10-year-old male patient diagnosed with alagille syndrome.

**Results:**

- **First operative:**
  - Adult male right liver recipient
  - TIF: 417 min; ICT: 45 min. TOTAL: 462 min. Total bleeding 5000 cc
  - Girl left liver recipient
  - TIF: 660 min; ICT: 55 min. TOTAL: 715 min. Total bleeding 11000 cc

- **Second operative:**
  - Adult female right liver recipient
  - TIF: 621 min; ICT: 49 min. TOTAL: 710 min. Total bleeding 3800 cc
  - Recipient boy left liver
  - TIF: 744 min; ICT: 65 min. TOTAL: 809 min. Total bleeding 3000 cc

**Conclusion:** Liver transplantation with the SPLIT technique is an option to expand the pool of donors and is a reality in our country, hoping to make further progress in order to continue helping our patients on the waiting list.

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P9.46

**Transition From Pediatrics to Adults: How Adolescents With Solid Organ Transplantation Move to Adult Care in a General Hospital**

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**Objectives:** To describe the experience of a transition program for solid organ transplant (SOT) patients from pediatric to adult care in a general hospital. To assess readiness for transition to adults using the validated TRAQ questionnaire.

**Methods:** A descriptive retrospective cross-sectional study of patients aged 16-24 years with a history of liver transplantation (LT) or renal transplantation (RT) attended at the Hospital Italiano de Buenos Aires in the period 2015-2019 was performed.

**Results:** A total of 157 patients were included, RT 69.4% (109) and LT 30.6% (48). 37% (59/157) [95%CI 32-42] of patients had participated in the transition program. Mean years of follow-up by the LT team of those who underwent transition was 11 years (SD 7.3) while those who did not undergo planned transition was 12 years (SD 7.2) and in the RT team it was 7.3 (SD 3.9) and of those who did not plan transition 9.3 years (SD 4.9) (p<0.01). The mean age at the beginning of transition in LT was 17.3 years (SD 1.5) and in RT was 20.7 years (SD 2.4) and the mean age at the end of transition was 21.5 in LT (DS 1.8) and in RT was 22 years (SD 2.4). Sixty-four percent of those who transitioned (57/89) had a record of the problem “Transition from pediatrics to adults” and 90% (53/59) had a record of the transition process in the medical electronic registry. The most frequent transition strategy was shared Clinic with the pediatric and adult care time in 96% (57/59). Forty-four percent of patients participating in the transition program (26/59) had the TRAQ questionnaire loaded in the medical electronic registry. The median ordinal TRAQ was 4 (between 3 and 4). The adult stay rate was 87% (51/59), there were no non-relevant adult emergency consultations and the median number of professionals consulted before reaching the referring physician was 1 (SD 0.67).

**Conclusions:** This study evidences the need to form planned transition programs together with the use of validated tools to measure the autonomy and responsibility skills of young adults with medical chronic conditions, capable of making informed decisions about their future health.
P9.47

**FIPS Score as a Predictor of 30-Day Mortality After Liver Transplantation – A Comparison With Validated Risk Scores (SOFT and BAR) in a Brazilian Cohort of Patients**

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**Introduction:** The novel Freiburg (FIPS) score was developed as a risk stratification and outcome prediction for patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) – using patient age, bilirubin, creatinine and albumin. Model for end-stage liver disease (MELD) was originally developed with the same principle, after it was validated for liver allocation, incorporated the sodium levels (MELDNa) and finally was not useful to predict mortality after liver transplant. Identification of high-risk patients is an important marker of quality for public policy. Therefore, the aim of our study is to evaluate this score as a predictor of surgical (30-day) mortality post liver transplantation when compared with previous validated scores.

**Method:** retrospective study that compared four prognostic scores [Balance of Risk Score (BAR), MELDNa, Survival Outcomes Following Liver Transplantation (SOFT) and FIPS] in 131 patients (mean age 51.5±11.9 years; 25.95% female) submitted to primary liver transplantation between April 2016 and February 2021 in a Brazilian cohort of Hospital do Rocio. Acute liver failure etiology was excluded. A receiver operating characteristic curve (ROC), with its area under (AUROC), was built to investigate the best observation of the prognostic scores. The scores were splitted into quintiles. Youden index was used to determinate the best cut-off point for the risk index.

**Results:** surgical mortality occurred in 24.43% (n=32) patients. Mean FIPS (0.51±1.10); BAR (8.39±3.87); MELDNa (21.43±8.04) and SOFT (10.41±7.44). Originally high risk patients (FIPS>0.92) didn’t presented higher mortality (p=0.29). SOFT score represented better the observation as the area under the curve (AUROC) was 0.81; with MELDNa (0.65); FIPS (0.65) and BAR (0.69) showing a not useful diagnostic accuracy. The best cut-off point for SOFT was in the second quintile (9-12).

**Conclusion:** Although not developed for this purpose, FIPS underperformed SOFT score as a prognostic index of 30-day mortality following liver transplantation in a brazilian cohort.

P9.48

**A Systematic Review of the Use of Patient-Reported Outcome Measures (PROMs) in Adults Undergoing Liver Transplantation**

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**Background:** Improved survival rates of liver transplantation (LT) (~80% 5-year survival) has shifted the focus towards reducing symptom burden and improving quality of life, which can be assessed using patient-reported outcome measures (PROMs). This study systematically reviewed measurement properties of PROMs to serve as an evidence base for the selection of suitable PROMs and offer new benchmarks for value-based health-care in LT.

**Methods:** MEDLINE, EMBASE, PubMed and COCHRANE databases were searched for relevant articles. Studies were included if they reported PROMs in LT candidates and/or recipients. Articles including patients <16 years only and clinician-assessed instruments were excluded. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist was used to assess methodological quality of included studies and measurement properties.

**Results:** The full-texts of 185 out of 2040 studies were reviewed. The Short-Form-36 (SF-36) (n=86 studies) and Hospital Anxiety and Depression Scale (HADS) (n=16 studies) were the most commonly reported generic instruments in this population. Only 15 studies provided original measurement properties for 24 PROMs. Both SF-36 (n=2 studies) and HADS (n=2 studies) showed high quality evidence for sufficient internal consistency (Cronbach’s alpha >7.8 and >7.3, respectively), but indeterminate reliability. The Liver Disease Quality of Life Questionnaire and its short version ((SF-)LDQOL) were the most used disease-specific PROMs reported in LT candidates (n=8 studies), and showed moderate quality evidence for sufficient internal consistency and construct validity in 2 studies. Five individual studies reported newly developed PROMs for LT recipients, often incorporating questions from existing instruments. These showed generally high quality evidence and sufficient internal consistency.

**Conclusion:** In addition to well-established PROMs (SF-36 and HADS), we conclude that the (SF-)LDQOL is the most promising for the detection of disease-specific changes in LT candidates. However, this instrument should be evaluated further for LT recipients.
Efficacy and Long-term Prognosis of Liver Transplantation For Porto-Pulmonary Hypertension

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Objective: Porto-pulmonary hypertension (PoPH) refers to pulmonary hypertension based on severe portal hypertension. Severe PoPH has a very high perioperative mortality rate and is still considered a contraindication for liver transplantation (LT). We analyze efficacy and long-term prognosis of liver transplantation for porto-pulmonary hypertension from our center.

Methods: A retrospective analysis was performed on 5 patients with PoPH who received liver transplantation in Beijing Friendship Hospital from January 2013 to March 2022, in order to analyze postoperative follow-up results and long-term survival.

Results: Five patients with PoPH with a mean age of 35.6 ± 18.6 years (60% females), were included in the analysis. Their primary diseases were hepatic spongioisis, Caroli disease, hepatitis B cirrhosis, drug-induced cirrhosis and primary sclerosing cholangitis. All patients were measured by Swan-Ganz catheterization of right heart, among them, the mean of the highest mean pulmonary artery pressure (mPAP) level measured under echocardiography was 46.6 mmHg (27-58 mmHg). The mean of their highest systolic pulmonary artery pressure (SPAP) were down to normal, and other patients still on medication. Operations went smoothly, except in one case where pulmonary artery pressure (mPAP) <35 mmHg, that can achieve surgical indications before LT. The Liver Transplant Center, Beijing Friendship Hospital, Capital Medical University, Beijing, People's Republic of China; 2Department of Critical Liver Diseases, Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, People’s Republic of China; 3Liver Research Center, Beijing Friendship Hospital, Capital Medical University, Beijing, People’s Republic of China; 4Clinical Center for Pediatric Liver Transplantation, Beijing Friendship Hospital, Capital Medical University, Beijing, People’s Republic of China; 5Department of Anesthesia, Beijing Friendship Hospital, Capital Medical University, Beijing, People’s Republic of China; 6Department of Ultrasound, Beijing Friendship Hospital, Capital Medical University, Beijing, People’s Republic of China.

Conclusions: Patients with pulmonary vasodilator therapy before LT can have excellent long-term outcomes post-transplant. Oral pulmonary vasodilator therapy can be effective treatment to quality patients for LT.

Novel MLTR Classification of Portal Vein Thrombosis For Purposes of Liver Transplantation

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Objective: Portal vein thrombosis (PVT) is a common complication of decompensated liver cirrhosis and occurs in 0.6-26% of patients on waiting lists. In a population of patients with liver cirrhosis, PVT develops within a year in 4.6-12.8%, in 10.2-20% within 5 years, and within 8-10 years in 38.7%. The Liver Transplant Center of the Skifosovsky Institute in Moscow is the leading transplant center in Russia, which performs liver transplants for portal vein thrombosis - such patients occur on the waiting list of the center up to 30%. The practice of the center led to the need to create its own classification, which would allow making decisions on the waiting list and intraoperatively.

For the purposes of liver transplantation, especially if transplantation is planned from a living related donor, it is possible to propose a classification of portal vein thrombosis that would be applicable to address tactical issues in liver transplantation. A variant of such a classification, which may be called MLTR, is given in Table 1. Visually, the classification is presented in fig. 1.

The developed classification was introduced into the work of the liver transplantation center of the N.V. Skifosovsky. The clinical material consisted of 650 patients of the liver transplantation center of the N.V. Skifosovsky operated from 2000 to 2020. Patients with PVT MOLOT1R0 accounted for 25% of the total number of patients, with M1L0T2R0 - half, with M1L1T2R0-1 - 25%. Based on the developed classification, the tactics of surgical treatment of patients was determined as follows. The developed classification was used to determine intraoperative tactics. In the presence of M1-2L0-1, the retropancreatic portal vein and its confluence were mobilized, for which the head of the pancreas was mobilized. This technique made it possible in some cases to perform erosion thrombintomyectomy without performing plastic or bypass interventions. In the presence of T3, thrombintomyectomy was not performed; it was planned to perform shunting or prosthetics of the portal vein. The presence of R1-2 prior to transplantation was of little hemodynamic significance. Thus, we can conclude that the developed classification was used by us to make a decision during liver transplantation.

The authors would like to thank Maria Kozhevnikova for her help in illustrating our work.

TABLE 1.

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<td>Thrombosis of the splenic veins</td>
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<td>Thrombosis of the branches of the portal vein</td>
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In the presence of calcification, the letters ca are added, in the presence of cavernous transformation ct.

In the presence of calcification, the letters ca are added, in the presence of cavernous transformation ct.
Single-Cell RNA Transcriptomics Reveals Dysfunction of Hepatic Lymphatic Endothelial Cells in Hepatitis B-Related Acute-On-Chronic Liver Failure

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Introduction: Acute-on-chronic liver failure (ACLF) is an acutely decompensated cirrhosis syndrome with high short-term mortality. Chronic hepatitis B virus (HBV)-related ACLF accounts for >80% of all cases in China, which places a tremendous burden on the health care system. Lymphatic system plays an important role in chronic liver diseases, such as cirrhosis, liver transplantation and hepatocellular carcinoma. However, very little is known about the relationship between the lymphatic system and ACLF. Here, we explored the role of hepatic lymphatic endothelial cells (LyECs) and lymphatic vessels (LVs) in ACLF with the help of single-cell RNA-sequencing (scRNA-seq) technology.

Methods: This study involved 25 human liver samples: 5 from healthy controls (HCs), 10 from cirrhosis patients, and 10 from ACLF patients. Liver damage and inflammation were assessed by H&E staining and plasma markers. After isolating hepatic non-parenchymal cells (NPCs), we analyzed subpopulations of NPCs by scRNA-seq, including KEGG pathway analysis and Ligand/receptor analysis. Intrahepatic LVs were evaluated by immunohistochemical staining. Tube formation assay was done to assess LyECs functions.

Results: ACLF exhibited more severe injury and inflammation to the liver than cirrhosis, as indicated by significant increases in plasma levels of alanine/aspartate aminotransferases and total bilirubin. Compared with cirrhosis cases, the number of intrahepatic LVs was decreased significantly in ACLF patients. scRNA-seq revealed many monocyte/macrophages infiltrating into the liver of ACLF cases. Meanwhile, scRNA-seq revealed a group of apoptotic and dysfunctional LyECs, which were the result of secreted phosphoprotein 1 (SPP1) released from infiltrating monocyte/macrophages. In vitro, SPP1 increased the proportion of dead LyECs significantly and impaired the ability of tube formation of LyECs in a dose- and time-dependent manner.

Conclusions: ACLF is associated with less LVs and LyECs dysfunction at least in part mediated by SPP1 released from infiltrating monocyte/macrophages. Hepatic LVs and LyECs can be a novel therapeutic strategy for ACLF.
P9.52
Role of Circulating Tumour Cells in the Management of the Liver Transplant Patient With Hepatocellular Carcinoma
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Introduction: For hepatocellular carcinoma (HCC), liver transplantation (LT) is considered a curative treatment, however, more than 10% of transplant recipients have recurrences within the first year. This suggests the existence of circulating-tumor-cells (CTC) that spread from a primary tumor and travel to peripheral blood and distant organs. Their detection and monitoring could be of great clinical value to an early prediction of recurrence as a real-time liquid biopsy. The aim of this study is to determine the relationship between CTC and clinicopathological variables and to compare the CTC-levels in patients with HCC before transplantation and at one and two years after surgery.

Methods: Peripheral blood was obtained from 34 patients with HCC included in the LT list. Immunomagnetic isolation of CTC was performed by the IsoFlux® System. Cell enrichment was stained with anti-CK, Hoechst-33342 and antiCD45, performing cell counting under a fluorescence microscope. The clinicopathological variables (number of tumors, vascular invasion, tumor necrosis and recurrence) were collected. Spearman’s rho, Mann-Whitney and Wilcoxon test were used.

Results: We found statistically significant differences in the CTC-levels between patients with vascular invasion and those without (U=6; p=0.005) such that patients with vascular invasion had median levels of 539 CTC/10 mL (IR:448-1768) and those without vascular invasion had median levels of 3 CTC/10 mL (IR:0- 31.25). Also we found that the serum levels of PIVKA-II were positively correlated with the tumor volumen and a higher clinical stage. Also we found that the serum levels of PIVKA-II increased significantly both at 6 months (Z= -2.814; p=0.005) and 1 year (Z= -2.315; p=0.021) after LT.

Conclusions: The median CTC-levels of the patients included in the study showed a downward trend after liver transplantation. Also, a significant difference was found in the levels of pre-transplant-CTC between patients with and without vascular invasion, these levels being significantly higher in patients with vascular invasion compared to those without vascular invasion. Detection of CTC may have a useful clinical implication in predicting the evolution of HCC after LT.

P9.53
Clinical Relevance of Pivka-II After Liver Transplantation For Hepatocellular Carcinoma
Felipe Alconchel1,2, Francisco Villalta2, Luis Sáenz2,3, María Isabel Sánchez-Lorénico2, David Ferreras1,2, Pedro Antonio Cascales-Campos1,2, Beatriz Febrero1,2, Laura Martínez-Alarcón1,2, Marta Jover1,2, Francisco Sánchez-Bueno1,2, Ricardo Robles-Campos1,2, Pablo Ramírez1,2.
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Introduction: Measurement of fetoprotein (AFP) level is already used widely for routine surveillance and noninvasive HCC diagnosis and to evaluate prognosis and monitor recurrence. Serum prothrombin induced by the absence of vitamin K or antagonist-II (PIVKA-II) measurement more specifically differentiates HCC from other hepatic diseases. The objective of the current study was to assess clinical utility of PIVKA-II in patients with HCC.

Methods: Peripheral blood was obtained from 46 patients with HCC before transplantation (LT), at 6 months and 1 year post-LT. Serum PIVKA-II-levels were determined by Lumipulse G1200 (Fujirebio®) and serum AFP levels were obtained in Cobase601 (Roche Diagnostics®). The main clinicopathological variables were collected. Tumor size refers to the diameter in centimeters of the largest lesion at diagnosis as determined by pre-LT imaging. Spearman’s rho, Mann-Whitney and Wilcoxon test were used.

Results: Regarding the association between PIVKA-II and the other parameters, we found a statistically significant association with tumor size (rho=0.423; p=0.003). We also found significant differences in PIVKA-II levels between patients with tumor size ≤3 cm (median=74,50 mAU/mL; IR 37,50-155) and >3 cm (median=372,50 mAU/mL; IR 45,25-1422), such that median levels in patients with tumor size >3 cm were significantly higher (U=92; p=0.003). We also found significant differences in PIVKA-II levels between patients with tumor size >3 cm (median=372,50 mAU/mL; IR 45,25-1422), such that median levels in patients with tumor size ≤3 cm were significantly higher (U=92; p=0.003).

Conclusions: PIVKA-II levels were positively correlated with the tumor size, suggesting that PIVKA-II may play a role in predicting the severity of the disease. A higher concentration of PIVKA-II may suggest a larger tumor volumen and a higher clinical stage. Also we found that the serum levels of PIVKA-II in HCC patients before and after LT had a significant difference, suggesting that PIVKA-II may be used as an indicator in evaluating curative effects of liver cancer surgery.
Graft Versus Host Disease Following Liver Transplantation: A Serious Complication

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Introduction: Graft-versus-host-disease (GVHD) after liver transplantation (LT) is a severe complication with high mortality rate (85%). Risk factors, diagnosis and management is challenging. Donor T-lymphocytes play a main role in the immunological attack against the host. We report a case and a comprehensive review of the literature. Around 160 patients are reported in literature with an estimated incidence of 0.5 to 2% of liver transplant. Liver transplantation from hepatocellular carcinoma (HCC) and alcoholic liver disease seems to be the main prevalent diagnosis of patients who developed GVHD.

Method: We present a 62-years old male patient with hepatitis C-virus (HCV) cirrhosis and successfully downstaged to Milan criteria HCC. Orthotopic liver transplantation was performed after 6 months of surveillance and discharged uneventfully after 7 days. One month later patient developed abdominal cramps, diarrhea and cutaneous erythema. Mild leukopenia with normal liver and renal function, blood and stool samples were negative, clostridium and other pathogens were also ruled out. Abdominal CT-scan showed moderate distal ileum and colon wall edema. At colonoscopy stellate ulcers was found, biopsy was taken as well to skin lesions. Colon biopsy showed acute inflammation with severe mucosal damage and apoptosis. Skin biopsy showed interphase vacuolar dermatitis. GVHD was suspected and donor lymphocyte chimerism was positive with 5%.

Results: Methylprednisolone was initiated then anti-thymocyte globulin and adalimumab were added. Bacterial, viral and fungal prophylaxis were given. The patient recovered and discharged in good conditions. Five months later the patient developed acute severe pneumonia with extensive lung necrosis that required mechanical ventilation but progressed to refractory respiratory distress and the patient died after 6 months following liver transplantation.

Conclusion: This is the first GVHD case after liver transplantation reported in Mexico. The diagnosis requires a high level of clinical suspicion. There is no strong consensus about the best management, but literature agrees that steroids, IL-2 antibodies, alpha-tumor necrosis factor inhibitors and antibiotics for opportunistic pathogens must be considered.
P9.55
The Role of Interventional Radiology in the Management of Early Vascular Complications After Liver Transplantation
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Introduction: Hepatic vascular complications after liver transplantation (LT) is a serious condition, which often results in graft failure and can lead to patient deaths. Early diagnosis and treatment of vascular complications provide prolong graft survival, and prohibited further complications. This study presents our experience of using endovascular treatments during the first week after liver transplant.

Method: 238 liver transplantsations were performed in a single center between 2012 and 2021. In 59 patients out of 238 liver transplant patients (37 men; mean age 27 ± 2.9 years); early endovascular interventions were carried 1 to 7 days (mean 2.7day ±0.24) after surgery. Doppler ultrasound was used in all cases, and computed tomography angiography was used in needed cases. Patients with vascular complications were grouped by arterial, venous, portal, and bleeding complication. In addition, arterial complications were sub grouped by occlusive (Hepatic artery thrombosis (HAT)) and non-occlusive (Hepatic artery stenosis (HS)/Splenic Artery Steal Syndrome (SAS)). The median follow-up period was 47± 4 month (range: 1 to 96 month).

Result: Seven patients had an arterial complication which was consisted of 5 HAT and 2 HAS. Five patients with hepatic artery thrombosis, intra-arterial thrombolysis was performed through the catheter. In two patients, continuous thrombolysis was performed to lyse the thrombus. The percutaneous transluminal angioplasty (PTA) was performed in all patients. Two of five HAT patients, stents were placed after the insufficient PTA. Two of these patients developed new stenosis and treated with repeat PTA.

Thirty-six patient’s diagnosis with SAS were treated by selective arterial embolization with coil devices. Angiographically, all SAS cases have demonstrated an increase in the hepatic arterial caliper and parenchymal perfusion after the treatment.

Five patients had been diagnosed with hepatic venous outflow obstruction. Two of the five patients were treated with balloon angioplasty, and three of them stents were used for insufficient flow after the balloon angioplasty. In four patients, active bleeding was embolized by endovascular intervention with coils or glue. No rebleeding was observed on follow-up. One patient with portal vein stenosis was observed after the LT and was treated with stent insertion.

During the follow-up period, the patient survival rate was 76, 3% (45/59).

Conclusion: Early endovascular intervention is feasible and safe in hepatic vascular complications following liver transplantation and also achieves a high success rate with the advance in interventional radiology.

P10.01
How Did the War Affect Organ Transplantation in Syria?
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Since 2011, the Syrian conflict has destroyed much of the country's infrastructure. The deteriorating humanitarian situation has involved health workers and facilities. In 2010, before the war, 385 kidney transplants were performed in Syria. This number declined to 154 in 2013 (65% less) before increasing to 251 transplants in 2018, which is still 35% less than the number of transplants performed before the war. In addition, the number of operational kidney transplant centers has decreased from 8 in 2010, distributed over 3 cities, to only 4 in 2013, all located in Damascus, which increased to 6 centers in 2019. Interestingly, with regard to type of living donor, the percentage of unrelated kidney donors has decreased by 20% for unclear reasons. Another alarming statistic is that more than 50% of kidney transplant physicians and surgeons are no longer practicing transplant medicine in their centers, either because they have left the country or because their centers had become nonoperational. Since the war, free and timely provision of immunosuppressive drugs for all patients in all provinces has been a leading challenge for health authorities and transplant patients. This difficulty has led to adverse medical consequences for patients. A project to initiate liver transplant came to a halt because of complex reasons but mainly because foreign trainers could not visit Syria. Although the autologous bone marrow transplant program had slowed until recently, it has become more active, involving both autologous and allogeneic transplants. The deceased-donor program is still not available in Syria; the war has just reinforced the many reasons that prevented the start of this program before the conflict. The commitment of transplant teams despite these large challenges continues to be extraordinary. The Syrian conflict has affected all aspects of organ transplant, paralyzing new projects and negatively affecting existing programs.
P10.02
Dapsone Induced Hemolytic Anemia in Solid Organ Transplant Recipients With Normal G6PD Activity
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Purpose: Pneumocystis jirovecii Pneumonia (PJP) is a life-threatening infection in solid organ transplant recipients. Trimethoprim-sulfamethoxazole (TMP-SMX) is the first line regimen. For people who are intolerant to TMP-SMX, Dapsone is a commonly used alternative. G6PD deficiency should be ruled out before initiation of Dapsone to avoid hemolytic anemia. However, Dapsone associated hemolytic anemia with normal G6PD activity has been reported in HIV patients as well as solid organ transplant recipients. We present a case series of 6 transplant recipients who developed hemolytic anemia after initiation of Dapsone despite normal G6PD activity.

Methods: We identified 6 organ transplant recipients with normal G6PD activity who developed anemia after initiation of Dapsone for PJP prophylaxis. Anemia workup include iron studies, vitamin B12, folate, reticulocyte count, haptoglobin, LDH, gastrointestinal, and other anatomic blood loss.

Results: All 6 patients had elevated reticulocyte count consistent with hemolytic anemia. Two patients had persistently low haptoglobin but no other signs of microangiopathic hemolytic anemia. There was no substrate deficiency or blood loss. After discontinuation of Dapsone, hemoglobin improved back to baseline without blood transfusion. For summary of cases, see Table.

Conclusions: Dapsone associated hemolytic anemia can occur in solid organ transplant recipient with normal G6PD activity. It is important to monitor hemoglobin within the first 3 months of Dapsone initiation. Blood transfusion is usually not required. The pathophysiology of Dapsone associated hemolytic anemia requires further studies.

P10.03
Alternative Surgical Techniques for Abdominal Wall Graft Donation to Guarantee Abdominal Wall Closure in the Donor
Clara Fernández1, Blanca Otero1, Luis Carlos Jiménez1, Carmelo Lozán1, Alberto Marcaccuzo1, Óscar Caso1, Alejandro Manrique1, Álvaro García-Sesma1, Félix Cambra1, Jorge Calvo1, Rosa González1, Victoria Carmona1, Iago Justo1.
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Introduction: Twenty percent of intestinal transplant recipients will require a surgical alternative to conventional primary abdominal wall closure. Abdominal wall transplantation is a developing technique that is increasingly performed for this purpose in isolated intestinal or multivisceral recipients, however, adequate closure of the donor is paramount, while simultaneously obtaining a large enough graft. The aim of this study is to describe alternative surgical techniques for closure of the donor, in cases in which abdominal wall graft extraction hinders subsequent donor abdominal closure.

Method: We describe the cases of two young donors in whom intestinal extraction was not carried out and in whom wall closure was not feasible, following standard techniques after abdominal wall graft extraction. We performed two different procedures to obtain adequate closure.

1. Hemi-fascia and hemi-abdominal wall graft extraction: It is an option when the recipients require an extension of the abdominal aponeurosis, yet have enough skin to guarantee skin closure. The perfusion of both epigastric arteries is needed. The remaining cutaneous half is used for closing the donor’s abdomen.

2. Hemi-abdominal wall graft extraction: Full-thickness abdominal wall is harvested from the donor, selecting the most vascularized half. It is an alternative for recipients that need a skin implant in addition to an aponeurosis extension. This option should be used for recipients that do not require a large fascial graft, but do require a significant cutaneous graft. The non transplanted half of the abdominal wall is used for donor closure.

Result: Abdominal wall transplantation allows for expansion of the abdominal cavity in organ recipients, and reduces the risk of compartmental syndrome and subsequent ischemia. However, the donor wall defect must be considered. The choice of donation technique was based on the magnitude of the defect in the donor as well as the size of defect to be covered in the recipient, while ensuring a tight and complete closure of the donor’s abdomen.

Conclusion: Abdominal wall graft extraction can be performed using non-conventional techniques that account for the extend and type of coverage needed by the recipient, while guaranteeing proper closure of the donor.
P11.01

Increasing the Consent for Brain Death Donor Family Members

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Introduction & Purpose: Mongolia’s Donor Law was first adopted in 2000 and amended in 2012 and 2018 respectively. The Regulatory department cells, tissues, and organs transplantation of the Center for Health Development has been established in 2018. There are 3 donor hospitals and 2 transplantation hospitals in Mongolia. Our department gets information daily from the donor hospital’s brain death diagnosis committee, if there is a donor with brain death, we make consultations with family members. It may be rejected because of religion, superstition, or personal opinion. Changing such factors will increase the number of family members’ consent and the number of transplantations.

Method: The study included 20 family members of the last three years approved by the brain death diagnosis committee for 3 Donor Hospitals.

Result: After meeting with those 46 family members, 26/65% of them accepted and 20/35% of them denied. Organ harvesting of 29 kidneys and 20 livers was successfully done from 23 out of 26 consented donors and thus saved 49 lives. The reasons for the rejection of family members are lamas/5 families/, shaman/5 families/, family opinion/3 families/ and lack of information about this/7families/.

Conclusion: From these, we could say that having knowledge about organ donation is increasing the likelihood of approval of becoming a donor. Therefore, it is important to meet with the religious representatives, which is one of the major opposing factors in order to give a proper understanding of donations to the public.

P11.02

Application of Ex-vivo Normothermic Machine Perfusion To Assess Renal Allograft Viability Following Renal Vein Thrombosis

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Background: Ex-vivo Normothermic Machine perfusion (NMP) has been shown to improve transplantation outcomes and assess the viability of discarded grafts. We report an application of NMP in assessing renal allograft viability in a case of renal vein thrombosis (RVT) following deceased renal transplantation in the immediate postoperative period.

Method: A 44-year-old female patient of unknown cause chronic kidney disease, on maintenance haemodialysis since 2018, underwent a deceased donor renal transplant from a young adult male donor after negative virtual crossmatch with CIT of 7 hrs 8 min. She had a history of fistula failure on multiple occasions and one abortion; her pro-coagulant workup was negative. She was on peritoneal dialysis for the past year, and she had multiple anti-HLA antibody specificities in class I and II loci (highest MFI 9700). She received Induction ATG, tacrolimus, mycophenolate, and steroids. The surgical procedure required reconstruction of the right renal vein. Allograft function was immediate and good with nadir creatinine 1.0mg/ml on postoperative day 6. On day 7, she had rapid onset anuria. Ultrasonogram showed clots in the graft pelvis with flow reversal, and CT angiogram showed RVT. On surgical re-exploration, the graft was congested, and the renal vein had an occlusive thrombus. After explantation and thrombectomy, the graft was placed on the Organ AssistTM using a red cell-based perfusate. It was perfused for six hours to check for graft viability on which there was the restoration of blood flow as evidenced by improving vascular resistance (peak 3mmHg/ml/min dropping to 1.3mmHg/ml/min) and blood flow (20ml/min rising to 220ml/min) and stabilization of lactate levels with a good macroscopic appearance. However, there was persistent haemorrhagic urine output despite an adequate and steady increase in renal blood flow.

Result: Despite demonstrating viability on NMP, the allograft could not be re-implanted due to haemorrhagic urine output on NMP, given the potential for bleeding and the hemodynamic instability in the recipient. The recipient was discharged on day 18 on dialysis. The allograft nephrectomy specimen showed isolated vascular acute T cell-mediated rejection- C4d negative with superimposed venous thrombosis.

Conclusion: EV/NMP can help decision making in complex situations where graft viability assessment is not readily apparent. Received Funding from PGIMER Chandigarh.
Access to Kidney and Liver Transplantation in the Adult And Pediatric Population: Interference of Argentine Legislation

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Introduction: In Argentina, the activity of donation and transplantation of organs, tissues and cells is regulated as a whole and in particular, by Law No. 27,447 enacted on July 4, 2018, and its Regulatory Decree No. 16/2019. This legal body empowers the National Institute for the Coordination of Ablation and Implantation (INCUCAI) to set the regulations for the donation and transplantation process in Argentina. The objective of the work is to compare the access to kidney and liver transplantation in the adult and pediatric population, but addressing the issue from a legal approach, its legal framework, bioethical principles as a foundation and its link with supra-legal law. Likewise, we will analyze the relationship between the various internal laws that regulate the matter, taking into account its normative hierarchy and harmonic interpretation.

Method: The current regulatory framework for transplant activity in the pediatric population was examined, in accordance with the Resolutions issued by the INCUCAI. Furthermore, a retrospective analysis was performed on transplant accessibility for kidney and liver transplantation in pediatric and adult patients for the period 2017 – 2020. The percentage of transplant accessibility indicates a waitlist candidate’s likelihood of receiving a transplant in Argentina. Data were obtained from the National Procurement and Transplantation Information System of the Argentine Republic (SINTRA).

Results: The percentage of transplant accessibility for kidney and liver transplantation in adult patients was 12, 15, 12 and 18% while in pediatric patients it was 73, 100, 98, 83 and 80% in the years 2017, 2018, 2019, 2020 and 2021, respectively. The analysis on accessibility to liver transplantation was, for the same period, in adult patients 7, 31, 32, 17 and 24% while for pediatric patients it was 77, 100, 95, 86 and 93%, respectively. For this period there were no differences regarding the criteria established by the regulations for the pediatric population.

Conclusion: The study of the Argentine registry shows a higher percentage of the pediatric population that accesses kidney and liver transplantation than the adult population, understanding that this phenomenon responds to the purpose pursued by the national regulations of prioritizing pediatric patients on the waiting list.
Monitoring of Organ Donation Potential From Brain Dead Donors in Polish Hospitals Using Web-Tooled System of Monitoring ICU Deaths WWW.Koordinator.net, Taking Into Account the Stratification of Hospitals With the Donation Potential

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Introduction: In order to be able to calculate the potential for organ donation from deceased donors in one hospital, region and country, it was necessary to develop a useful stratification system for all hospitals taking into account their characteristics in terms of having or not having wards crucial for donor identification and recruitment (ICU, Neurology, Neurosurgery), number of beds, patient profile (children vs adults).

Methods: There are 1032 hospitals in Poland, but only 388 have structural capabilities (minimum ICU and operating theatre). These hospitals with a potential for donation of the deceased were characterized according to the criteria presented above.

Results: The largest group were hospitals with ICU only for adults (161 hospitals), followed by hospitals with ICU and adult stroke units (76), hospitals for adults with ICUs with neurology department without stroke beds (25), hospitals for adults with ICU, stroke unit and neurosurgery. In the case of possible pediatric donation, the largest group were 5 hospitals with ICU departments for children, pediatric neurology and pediatric neurosurgery. The remaining hospitals were unique. In Poland, out of 388 hospitals with the potential to donate in terms of potential donors, only 120 hospitals were active (31%). ITUs in hospitals with a donation potential have 3,443 beds, including 327 beds in pediatric departments. Reports on deaths were retrospectively analyzed in terms of the possibility of diagnosing deaths according to neurological criteria and the detection of possible donations. In total, 1,116 reports from 105 hospitals were submitted to the ICT system in 2021. The donation potential analysis was carried out on the basis of 600 full monthly reports from 50 hospitals. Numbers and indices related to organ donation potential were calculated, both on the hospital and ICU scale: number of beds and admissions, total number of deaths, deaths from causes often fatal according to neurological criteria, number of brain death diagnoses and number of organ donors.

Conclusion: We treat the result of this study as fundamental for the calculation of the donation potential in Poland. Our thesis is that precisely characterized hospitals from the same group should have the same potential and should be active in the donation process on the same level. In hospital and ICU scales, the examined indicators showed: low frequency of brain death confirmation procedures in the total number of deaths in Polish hospitals, a high percentage of donations in the total number of dead brains, which may be due to the successful authorization of donation and the adoption of risky donors and organs by transplant teams, it may also be due to the fact that the procedures of the brain death protocol in Poland are used only in cases where organ donation is expected. It was possible to calculate the donation potential for individual groups of hospitals using the coordinator.net network tool.
P11.06

HTK vs WISCONSIN and Delayed Renal Graft Function

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Introduction: Preservation solutions are beneficial for solid organ transplants, being an important factor in the development of delayed graft function (DRF), being associated with a reduction in graft survival after one year.

Objectives: To compare the use of histidine-tryptophan-ketoglutarate (HTK) solution vs University of Wisconsin solution with the development of renal graft function delay (DRF).

Material and Method: Observational (Cross Sectional), retrospective and analytical study. Renal transplant patients with cadaveric donors were included during the period between January 2017 and December 2021. T test was used for independent samples and Chi2 2x2 for categorical variables. An alpha value of ≤ 0.05 was determined for statistical significance.

Results: 82 kidney transplant recipients were retrospectively compared with cadaveric, preserved HTK (n=49) and UW (n=33) donors. The mean age of the donors was 40 years. The incidence of DRF was 56%. In the Student test analysis, statistical significance was observed in donor age (37.31 vs 42.52 p=.035), donor BMI (25.78 vs 29.46p=.000), pre-ablation creatinine (0.94 vs 1.18 p=.014) and pre-ablation urea (28.86 vs 39.74 p=.006) and renal DRF.

In the CHI2 analysis, the use of HTK solution (KANTRILEX/ CUSTOPLEX) was associated with 40.2% renal DRF development (p=.012) (OR 3.17 95% CI 1.26-7.95), compared to UW solution (14.6%) (p=.007) (OR 0.28 CI 95% 0.11-0.71).

Conclusion: In our study, it was observed that the use of HTK solution was associated with a higher risk of renal DRF compared to UW solution.

P11.07

BMSCs Combined With Normothermic Machine Perfusion Resuscitate Aged Donor Liver With Long Warm Ischemia Time in Rats

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Background: Both aged and donation after cardiac death (DCD) donor liver, considered as marginal organs, were used for transplantation due to huge organ shortage in the world. Organs combined with both danger factors would impair the donor liver viability. Using normothermic machine perfusion (NMP), we investigated the possibility of mesenchymal stem cells (MSCs) to revive the aged DCD donor liver in a rat model.

Methods: The SD rats used for NMP were all over 14 months of age. BMSCs were isolated from the bone marrow of SD rats. Rats were anesthetized and cardiac arrest was induced by compression of the heart for 30 minutes as warm ischemia prior to donor liver harvesting. The liver was connected to a rat liver perfusion machine for NMP with or without 10^6 BMSCs infusion.

Results: The weight of the aged liver in the experimental and control groups was 23.03 ± 0.25 g and 21.40 ± 0.87 g. the donor liver appeared to multiple bruised foci in both prior- and post- perfusion, while liver with BMSCs perfusion had fewer bruised foci (Figure 1A, B). The pH was maintained between 7.35 and 7.45 in both groups during perfusion. Lactate in the BMSCs group decreased after 1 hour during perfusion and fell below 1 gradually within 3 hours, while in the control group it decreased more slowly and remained around 4 even after 4 hours of perfusion (Figure 1C). Pathological appearance showed that the pathological Suzuki’s sores of liver in the control group were higher than MSCs group, with bruised liver sinusoids, apoptosis and focal necrosis of hepatocytes. In contrast, pathological change in the liver of the BMSC group showed significant improvement with no obvious necrosis and structural integrity of the liver lobules (Figure 1D). The climbing rate and peak value of AST and ALT in the BMSCs group decreased after 1 hour during perfusion and fell below 1 gradually within 3 hours, while in the control group it decreased more slowly and remained around 4 even after 4 hours of perfusion (Figure 1E, 1F).

Conclusion: Our results demonstrate that the use of MSCs during normothermic machine perfusion is a feasible strategy to resuscitate the aged DCD donor liver.
International Registry in Organ Donation and Transplantation (IRODaT) – 2021 Worldwide Data

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Introduction: IRODaT is the first registry in this field, which contains statistics of deceased/living donors and transplants. Out of the 111 countries with organ donation or transplantation (D&T) activity, 86 national reporters have submitted data to IRODaT during the last 19 years.

Methods: Each participant country inserts their own data to the website and all data are validated. The information registered follows the definition of "The Critical Pathway of Deceased Donation (1)", ensuring uniformity throughout the registry and aiding correct interpretation of the data by the scientific community. The data could be verified contacting the official reporter when it is needed. The compilation of all this information worldwide can be accessed by the whole community.

Results: Currently twenty one countries have submitted the database from 2021 at the IRODaT registry. Although organ D&T rates mostly dropped as expected due to the emergency of COVID-19 worldwide, some countries had the highest improvement in deceased donation (DD) compared to 2020 data, such as: Spain (from 37.97 to 40.2 ppm), USA (from 38.03 to 41.88 ppm), Italy (from 21.6 to 22.52 ppm); Czech Republic (from 23.3 to 25.06 ppm), Argentina (from 9.82 to 13.13 ppm) and Iceland (from 13.33 to 29.35 ppm); while Australia, Austria, Denmark and Estonia reported a downward trend with 16 from 18 ppm; 20.26 from 23.9 ppm; 16.90 from 21.38 ppm and 15.79 from 24.83 ppm respectively. The increase in the DD activity of Saudi Arabia and United Arab Emirates is significant by 150% and 400% compared to the previous year. Regarding Brazil and Portugal preliminary data, the numbers collected included only the first semester of 2021 and are excluded in the figure 1.

Six countries have reported an increase in Donation After Cardiac Death (DCD type III) including Spain, the US and Italy, in which DCD donation represents more than 30% of their total number of deceased donations. Thus far, thirteen countries have reported living donation activity (LD) led by Saudi Arabia (37.4 ppm), the US (19.75 ppm) and Cyprus (11.59 ppm). The number of LD performed was affected significantly since many programs were deferred.

Conclusions: In 2021, the challenges hospitals faced, including restrictions, flight reductions and border closures affected national programs worldwide as reflected above. Nevertheless, coordination and transplant teams have minimized the impacts of the pandemic and while health resources were globally disproportionally affected, certain countries managed to increased D&T rates.

References:
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New Technique for the Extraction of Abdominal Wall Grafts

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Introduction: Difficulties in proper abdominal wall closure are frequent after multivisceral transplant, isolated intestinal transplant and some cases of liver transplantation, due to the loss of the abdominal content. Several methods have been published for primary closure of the abdominal wall. Examples include the use of biological meshes, separation of components, which is exceptional given the past history of multiple abdominal interventions in these patients, and finally, full thickness graft and non-vascularized fascia.

Methods: We describe a novel technique for full-thickness abdominal wall extraction, in which the abdominal wall is perfused synchronically with the rest of the abdominal organs. This technique minimizes the ischemic time and allows for a subsequent decision between using a full-thickness graft or non-vascularized fascia.

Results: We have performed six non vascularized fascia transplants in three intestinal transplant recipients, one multivisceral recipient and two liver transplant recipients. The size of the abdominal wall defects that we have covered with these grafts vary between 17x7 cm to 25x20 cm. Only one of the cases required multiple take-backs to the operating room and required a complete removal of the fascia graft. This patient, along with two more, ultimately died from sepsis. We were able to properly close all of the donors. On microscopy, all the fascial grafts showed less areas of necrosis and picnosis, as compared to those performed with the classic technique.

Conclusions: Our extraction technique allows for donation of a graft that allows us to close large defects in the recipients with non-vascularized fascia. Further studies are needed to prove the benefits of full-thickness grafts.

Changes of Brain Death Donors for Recent 10 Years in Korea (Based on Organ Transplantation Law)

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Abstracts

Background: Although the Korea National Organ Transplantation Law was enacted on February 9, 2000, the disparity between supply and demand was problematic with lack of organ donors. On June 1, 2011, 10 years after enacted Law, the establishment of independent organ procurement agency, Korea Organ Donation Agency(KODA) and obligatory reporting potential brain death(PBD) patients to KODA were amended. Accordingly, in the event of brain death, the donation was processed promptly and systematically. We analyze and report on brain death organ donation(BDOD) in Korea retrospectively for 10 years.

Methods: A retrospective analysis was conducted on 20,171 PBD and 5,047 BDOD notified to the KODA from 2011 to 2021.

Result: Notifications of PBD increased from 609 in 2011, recording the highest notifications to 2,484 in 2019, and notifications of BDOD was 2,141 in 2021. The number of BDOD increased from 368(pmp 7.2) in 2011 to highest 573(pmp 11.39) in 2016. Recently, it is showing a decreasing trend of 515 in 2017, 449 in 2018, 450 in 2019, 478 in 2020, and 442 in 2021(pmp 8.53). 67.8% of BDOD were male, which was more than female. The age groups mainly consisted of 28% in their 50s, 24% in their 40s, 15.4% in their 60s, and 12.3% in their 30s. The average age of them increased by 5.8 years over 10 years from 43.3 years old in 2011 to 49.1 years old in 2021, indicating that the upper age limit for donors is increasing. In 2019, the oldest brain-dead organ donor was 86 years old. The causes of brain death of BDOD were cerebrovascular system/stroke (40.9%), hypoxic brain injury (29.4%), head trauma (27.9%), central nervous system tumor (0.7%), and others 1% in order. As a result of analysis of the two periods from 2011 to 2015 and 2016 to 2021, it was cerebrovascular system/stroke (44.3%), head trauma (29.9%), and hypoxic brain injury (23.8%) in order from 2011 to 2015, but it was cerebrovascular system/stroke (38.4%), hypoxic brain injury (33.6%), and head trauma (26.5%) in order from 2016 to 2021, indicating that the proportion of hypoxic brain injury increased.

Conclusion: Even in the unique Asian cultural and ethical environment such as confucianism, BDOD has made great progress in Korea. The number of notifications of PBD and BDOD increased because of the enforcement of the amended law. However, it is currently stagnant because of various factors such as the enforcement of the 1 Act On Hospice And Palliative Care And Decisions On Life-sustaining Treatment For Patients At The End Of Life, implemented on February 2018 and the recent COVID-19 outbreak. In order to promote organ donations by BDOD in the future, it is required to prepare for a new leap forward for life sharing by strengthening the role of organ procurement organizations and by preparation of the groundwork for DCD implementation with the amendment of the law.
A New Designed Machine Perfusion System to Mimic the Cardiac Cycle’s Heart Function for a Better Hepatic Microcirculation Perfusion

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Background: Machine perfusion is a relatively new concept developed for protecting marginal liver transplantation. However, so far, limited studies have reported on liver transplantation donated after cardiac death (DCD). Objective: To establish and verify a novel machine perfusion concept to eliminate these risk factors and recover DCD livers.

Methods: To explore a novel hypothermic oxygenated perfusion (HOPE) system, two pumps and an elastic water sac were integrated into the perfusion system to mimic the cardiac cycle’s heart function. Compared to the other two traditional systems (HOPE S1 and S2), the novel HOPE system (HOPE S3) was verified in rats by no injured livers (perfused with methyl-ene blue diluted by UW-G) or DCD livers subjected to 60 min in situ warm ischemia, without application of heparin. Liver perfusion outcomes were compared using macroscopy, microscopy, molecular tests, and orthotopic liver transplantation (OLT).

Results: DCD livers, subjected to HOPE systems’ perfusion, disclosed reduced injury and improved survival compared to static cold storage after warm ischemia of 60 min (DCD+SCS). The post-transplantation survival rates of 4 weeks were 0%, 20 and 30% in DCD+SCS, DCD+SCS+HOPE S1, and DCD+SCS+HOPE S2 group, respectively. In contrast, HOPE S3 protected from hepatocyte and non-parenchymal cell injury and led to 60% (6/10) animal survival after 60 min of warm donor ischemia (DCD+SCS+HOPE S3). These data were further demonstrated by monitoring the hepatic sinusoid microcirculation, function morphological, and molecular changes of preserved livers.

Conclusion: The newly designed novel machine perfusion system achieved complete and homogeneous liver perfusion and is regarded as a useful tool for resuscitating DCD liver grafts with severe warm ischemic injuries. Key words: Liver transplantation; Hypothermic oxygenated perfusion; Donation after cardiac death; Organ recovery; Preservation injury; Ischemic reperfusion injury; Static cold storage; Hepatic sinusoidal; Hepatic microcirculation; Inferior vena cava.

Global and Country-Level Growth in Deceased Organ Donation Over Two Decades

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Background: Organ shortage remains the main challenge to organ donation and transplantation worldwide. Given the limited number of deceased donors (DD), consolidated efforts were made in the past two decades to legislate and facilitate brain death donation and further increase its public acceptance. To better understand the impact of these strategies, we describe the global and country-level change in deceased organ donation activities between 2000-2019.

Methods: Using data from the Global Observatory of Donation and Transplantation (GODT) for the years (2000 to 2019), we screened all WHO countries (n=194) and included 75 countries with available data on deceased donation activities (DD data for ≥ 5 years). We obtained the annual number of DD in each country, including donors after brain death (DBD) and donors after circulatory death (DCD), and reported in absolute numbers in addition to the adjusted per million population (PMP) numbers. The average annual percentage change (AAPC) in the number of donors PMP was calculated using the JoinPoint Software of the National Cancer Institute.

Results: In a sample of 75/194 countries with available data on deceased donation activities, the absolute number of DD increased by 265.3% (from 11181 in 2000 to 40841 in 2019), or 0.11 to 0.4 DD, PMP with an AAPC of 7% (95% CI [4, 10.1]). This increase was predominantly driven by the rise in DBD, which increased by 228.2% (from 9703 in 2000 to 31842 in 2019), or 0.1 to 0.32 DD, PMP with an AAPC of 6% (95% CI [4.6, 7.4]). However, temporal trends in the number of DD adjusted for the population varied considerably among countries (Figure 1), such that significant growth in DD was seen in 60 (80%) of the nations (AAPC 7.5%; 95% CI [5.6, 9.5]), while the remaining 15 countries were more likely to feature a decline over time (AAPC -1.6%; 95% CI [-3.1, -0.1]).

Conclusion: In this global sample, the number of DD increased by four folds between 2000-2019, mainly driven by donations after brain death. However, only 4 in 5 countries maintained growth in their deceased donation activities over time. Future research is needed to understand the variation in donation activities worldwide.

Figure 1: Country-level average annual percent change in the number of deceased donors

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Organization of Organ and Bone Marrow Donation And Transplantation in Poland

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The beginnings of transplant medicine in Poland date back to 1966, when the first transplantation took place (kidney from a deceased donor). Work on Polish transplant laws was launched in the early 1990s, when the Ministry of Health began to introduce legal rules concerning the procurement and transplantation of cells, tissues and organs. The Cell, Tissue and Organ Recovery and Transplantation Act was published in 1995 and came into force in March 1996. In the same year, the Polish Transplant Coordinating Center POLTRANSPLANT, was established as a national transplant organization in the field of organs and bone marrow. In 2021, we celebrated the 25th anniversary of the POLTRANSPLANT.

To the end of 2021 the total number of organ transplantations in Poland was 36,915. Kidney transplantation is the most common (26,941 including the number of transplantations from living donors - 9,689). Total number of transplanted livers was 5,637, including transplants of part of the liver from living donors - 431. From the first heart transplant in 1985 3097 hearts were transplanted. Also 436 lungs were transplanted in Poland, including 1 transplant from a living donor. Single face, upper limb, intestine and pancreatic islets transplants have also been reported. The number of organ transplantations from deceased donors places Poland in the middle among European countries.

The history of hematopoietic stem cells transplantation (HSCT) in Poland is shorter than that of solid organs. The first successful allogenic (related) HSC T in Poland was performed in 1983 and one year later the first autologous HSCT. Work on transplant medicine in Poland date back to 1966, when the first transplantation took place (kidney from a deceased donor). On arrival to the hospital on receipt of a transplant offer, recipients can be found to be unfit precluding transplantation. In this instance, the graft is offered back to NHS Blood and Transplant. Grafts often, however, remain locally to reduce cold ischaemic time inherent in further relocation. When another suitable recipient is not found, and cold ischaemic time (CIT) increases to undesirable levels, grafts can unfortunately be deemed unusable. The first transplantation took place (kidney from a deceased donor). On arrival to the hospital on receipt of a transplant offer, recipients can be found to be unfit precluding transplantation. In this instance, the graft is offered back to NHS Blood and Transplant. Grafts often, however, remain locally to reduce cold ischaemic time inherent in further relocation. When another suitable recipient is not found, and cold ischaemic time (CIT) increases to undesirable levels, grafts can unfortunately be deemed unusable.

Case Presentation: Herein we describe a case in which ex vivo normothermic perfusion (EVNP) facilitated the admittance of a third potential recipient for a 66yo DCDkidney. The first two allocated recipients who were deemed unfit: the first recipient was found to have an infected lower limb ulcer; the second patient was found to have raised inflammatory markers in the context of an aorto-bifemoral graft. At the third recipient (55yo, pre-dialysis) the CIT on the graft was 19 hours. The patient was admitted to the ward and EVNP was used to ‘pause’/limit CIT in order for the patient to be prepared, assessed and consented for transplantation. EVNP assessment score = 1 (one hour perfusion duration), with excellent perfusion demonstrated and good urine output (>100ml); total CIT was 23 hours at in situ reperfusion. The patient was successfully transplanted and the graft achieved primary function with a creatinine of 166µmol at time of discharge. At 5 months the creatinine is 151µmol and eGFR 32mls/min/m2.

Case Presentation: Herein we describe a case in which ex vivo normothermic perfusion (EVNP) facilitated the admittance of a third potential recipient for a 66yo DCDkidney. The first two allocated recipients who were deemed unfit: the first recipient was found to have an infected lower limb ulcer; the second patient was found to have raised inflammatory markers in the context of an aorto-bifemoral graft. At the third recipient (55yo, pre-dialysis) the CIT on the graft was 19 hours. The patient was admitted to the ward and EVNP was used to ‘pause’/limit CIT in order for the patient to be prepared, assessed and consented for transplantation. EVNP assessment score = 1 (one hour perfusion duration), with excellent perfusion demonstrated and good urine output (>100ml); total CIT was 23 hours at in situ reperfusion. The patient was successfully transplanted and the graft achieved primary function with a creatinine of 166µmol at time of discharge. At 5 months the creatinine is 151µmol and eGFR 32mls/min/m2.

Discussion: Without EVNP this graft would have likely been discarded. Cold ischaemic time was effectively paused by the perfusion technology allowing the graft to be assessed and utilised, and ultimately prevented graft discard. EVNP offers a technique to improve organ utilisation.
P11.15

DONASUR: Descriptive Analysis of 11 Years of Argentina’s Participation

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Introduction: DONASUR is the official registry of donation and transplant activity in Latin America and the Caribbean. Argentina, through INCUCAI, has participated since its inception. The project was presented in 2011 at the XXX Meeting of Health Ministers of MERCOSUR and was approved by the heads of the region’s national health portfolios. We propose to carry out a diagnosis of the situation on the participation of Argentina in creation, maintenance and growth over the last 11 years.

Methods: Descriptive study on the participation of Argentina in DONASUR between the years 2005 to 2021.

Results: Argentina began uploading data to DONASUR in 2013. Thanks to the computer system for administration, management, supervision and consultation of the activity of procurement and transplantation of organs, tissues and cells at the national level (SINTRA), it was able to retrospectively upload since 2005. SINTRA information was downloaded in Excel format and imported into DONASUR, with subsequent validation and quality control. Currently, a consolidated team within the Information Technology and Systems Directorate of INCUCAI is in charge of uploading data to DONASUR. Throughout 11 years of active participation, Argentina has entered 16 years of history, which translates into 17,106 donors, 41,432 transplants, 688 establishments throughout the country where ablations were performed and 229 where transplants are performed.

Conclusion: Argentina has managed to participate continuously thanks to a computer system that facilitates the search and upload of data, where SINTRA represents a fundamental tool for an efficient upload.

P11.16

Quality Monitoring Indicators in the Process of Organ And Tissue Donation for Transplantation: A Scoping Review Preliminary Results

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Introduction: Organ and tissue donation programs for transplantation are complex and have characteristics of a multifactorial nature, with regard to management and treatment. Given the importance of the availability of organs and tissues, as well as the aspects of measuring efficiency and effectiveness in this process, it is essential to evaluate, monitor and demonstrate the quality of these programs. However, there seems to be no consensus on the specific and sensitive indicators that should be used for this purpose. The objective of the study is to map and analyze the scientific literature on indicators for monitoring the quality of the organ and tissue donation process for transplantation.

Inclusion criteria: Studies that present the concept of interest were included: indicators for quality monitoring to assess the process of organ and tissue donation from brain-dead donors. Primary and secondary surveys were considered using any method, from white and gray literature and in any language, from 1980 to May 2021.

Methods: The review was carried out following the methodology proposed by the JBI for scope reviews. Databases, portals and directories searched include: MEDLINE (PubMed), CINAHL (EBSCO), Embase (Elsevier), Scopus (Elsevier), Web of Science (Clarivate Analytics), Business Source Complete (EBSCO), Virtual VHL Health Library; and gray literature were searched on Google Scholar, national and international theses and dissertation libraries and on the websites of organ and tissue donation and transplantation organizations and quality. Triage of studies was performed in pairs, paying attention to eligibility criteria. Data were extracted using specific variables and presented in categories according to the evaluative triad structure, process and result and by the pillars of quality proposed by Avedis Donabedian and the Institute Of Medicine (IOM), in the form of diagrams, tables, frames and narrative synthesis.

Preliminary results: 2,810 records were identified in databases, websites, portals and directories. Of these 2,249 (80.0%) records, titles and abstracts were read after the identification of duplicates, and 137 (4.9%) documents were included for the second stage of reading the full text. After reading and searching for references, 36 (1.3%) documents were included in the final result of the review. 405 mentions of quality indicators were identified, most of them published by Spain and the United States.

Conclusion: There is great variation in the nomenclature and definition of quality indicators in organ donation. A deficit was identified in the availability of information on the indicators.
**P11.17 Sustaining Life After Brain Death During Pregnancy: A Case Report**

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The brain death of a young pregnant woman is an event which poses several ethical and clinical criticalities for health professionals. During the first wave of COVID-19 pandemia in 2020, a 23-year old woman at 24 + 3 weeks of gestation was admitted in our Neurointensive Care Unit, for intracranial bleeding. At the admission the patient met the criteria for the diagnosis of brain death. On the arrival, the foetus was vital. Therefore, we proceeded to maintain the vital functions of the mother, aiming to provide the foetus with a chance for survival. The clinical treatment was performed around the following key concepts:

- Maintaining hormonal/metabolic functions:
  1. Thyroid: Levothyroxine 150 mcg firstly, raised to 200 mcg to sustain foetal growth;
  2. Steroid therapy with hydrocortisone which was first provided intravenously and then in a second phase via enteral nutrition as cortisone acetate 25 + 12.5 mg;
  3. Diabetes insipidus: firstly we use intravenous desmopressin boluses of 2 mcg x 3, which were then changed to continuous infusion with variable dosing 0.05-0.03 mcg/h (4-1 mcg/die), adjusted according to the polyuria level.

- Maintaining cardiovascular functions: the very early hormonal substitution and the correct fluidic management allowed to interrupt the aminic support within the first 72h of hospitalization, mitigating its impact on placental circulation.

- Nutritional support suitable to the growing organism at 25 Kcal/kg (plus vitamins, iron and other nutrients) and, after 10 days, at 30 Kcal/kg.

- Management of healthcare-associated infections: to reduce the risk of pulmonary infections an early tracheostomy (on day 2 of hospitalization) was performed; manoeuvres of bronchial de-obstruction were routinely performed. The patient developed a Ventilatory Acquired Pneumonia by Methicillin-Resistant Staphilococcus Aureus, which was treated with a short cycle of linezolid. The patient also developed a urinary tract infection by Escherichia Coli, which was treated with clavulanic-amoxicilline. Strictly antibiotic stewardship and infection monitoring were performed.

- Meticulous nursing and mobilization of the patient to prevent decubitus and thrombosis: the patient was routinely mobilized on alternating decubitis, including the left hip.

- Monitoring foetal well-being and intrauterine growth: the gynecologists monitored placental circulation constantly and never found any abnormality. The treatment, described above allowed the foetus to develop within the standards and a caesarean section was performed at 30 weeks of gestation (after 39 days of hospitalization); the child was born with weight of 1670 grams (90th percentile) and of length 44 centimeters (97th percentile). Following the birth, the child required intubation and respiratory support for 36 hours and surfactant administration, after which he was successfully extubated. As of the date of this abstract, the child shows a standard psychomotor development.

**P11.18 Allocating Deceased Donor Using Local vs Imported Renal Allografts: Logistics Are More Important Than Distance**

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**Background:** The deceased donor kidney allocation system (KAS) aims to optimize and equalize organ access for candidates nationwide and facilitate organ matching for candidates who are harder to match due to biologic reasons. In March 2021, UNOS implanted a new allocation of KT based on distance from the donor hospitals. A distance within 250 nautical miles will receive additional proximity points to access KT.

**Material and Method:** This was a retrospective single-center study assessing the Cold ischemic time (CIT) and Delayed graft function (DGF) in allograft kidneys January 2014 to December 2020. We studied 221 import KT and compared the outcomes to locally procured KT (n=160) and finally compared the patients and grafts survival rates in 1-year and 5-years.

**Results:** Donor and recipient demographics were similar in both groups. Induction and maintenance immunosuppression were similar in both groups. CIT was significantly higher in the imported group (27.6 vs. 15.9 hours, p< 0.0001). However, distance did not impact CIT significantly (p=0.07) in the imported KT’s. Distance also did not impact the rate of DGF in both groups (imported 21% vs. 22%, p=0.74). Patient and graft survival were similar in the imported vs. local group.

**Conclusions:** We conclude that distance alone has no correlation with CIT and DGF. There are many logistical factors and OPO factors that has significant impact on CIT which should take into consideration.

**Keywords:** Kidney, Transplant, New allocation, distance, Survival rate.

![Fig. 1](image1.png)

**Figure 1:** Cold Time (Hr) vs. Distance from Syracuse (miles)

**R^2 = 0.0731**

![Figure 2](image2.png)

**Figure 2:** DGF vs. Distance from Syracuse (miles)

**R^2 = 0.0016**
System-Level Barriers to Living Donor Kidney Transplantation: A Cross-Sectional Survey Study of Health Professionals

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Background and objectives: Living donor kidney transplantation (LDKT) is the preferred therapeutic option for patients with end-stage kidney disease and health professionals (HPs) can provide unique insights to improving the delivery of LDKT to patients. We aimed to quantify system-level barriers to LDKT that we have previously identified in our qualitative work and estimate their association with LDKT performance. We also aimed to determine if HPs' characteristics influenced responses and what HPs thought should be priorities to increase LDKT.

Methods: We conducted a cross-sectional survey of Canadian health professionals (HPs) and asked participants to rate statements on a Likert scale of 1-5 (strongly disagree-strongly agree). Statements captured themes related to communication, role perception, education/training/comfort, attitudes, referral process, judge, role as the barrier, and resources/infrastructure. The percentage of participants who agreed with these statements was analyzed and compared by LDKT performance (provincial living donation rates higher versus lower than the national average) and HP characteristics.

Results: We obtained 353 complete responses. Overall, themes related to poor communication, poor role perception and HPs education/training/comfort emerged as barriers to LDKT. When compared with HPs from high-performing provinces, those from low-performing provinces had lower odds of agreeing that their province promoted LDKT (aOR=0.27, 95%CI:0.16-0.48). They also had lower odds of initiating discussions about LDKT (aOR=0.30, 95%CI:0.17-0.55), higher odds of agreeing that the transplant team is best suited to discuss LDKT (aOR=2.64, 95%CI:1.60-4.33) and that more resources would increase LDKT discussions from them (aOR=2.06, 95%CI:1.25-3.40). When comparing responses by HP characteristics, non-physician role and <10 years of experience were associated with the level of agreement across several themes. Creating guidelines, streamlining evaluations, and improving communication were ranked as priorities to increase LDKT over patient education.

Conclusion: Poor communication between treating teams, poor role perception and HPs lack of education/training/comfort emerged as system-level barriers to LDKT and even HPs themselves identified addressing system-level inefficiencies as priorities to increase LDKT over patient education. More importantly, we report that poor role perception, low resources, and poor infrastructure may be driving differences in LDKT performance in a real-world setting. Our findings have policy implications and can build on the current patient-level work that others are pursuing to increase LDKT.

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P11.20
Detailed Analysis of Autopsy in Brain Death Donation in Korea

Ki Dong Song1, Ji eun Min2, Yong min Lee3, Kyoung min Kim4, Hyunjin Kang1, Jeong rim Lee2, Insung Moon3.

Background: In Korea, in the case of an unnatural brain death donor who has agreed to donate organs, it can be proceeded only after obtaining approval from the examination before autopsy. If an autopsy is deemed necessary during the process, the donation procedure is stopped contrary to the intention of the donor and the bereaved family. Therefore, we would like to find out a way to respect the will of the noble family who decided to donate through the analysis of the brain death organ donor, which was discussed for autopsy from 2016 to 2021.

Method: From January 1, 2016 to December 31, 2021, among 1,437 exogenous brain death donors who agreed to donate organs, 51 patients for whom autopsy was discussed were analyzed.

Result: From 2016 to 2021, there were 2,907 brain death donors, of which 1,437 (49.4%) were unnatural death. As for diseases caused by external factors, 788 cases (54.8%) of head trauma, 645 cases (44.9%) of hypoxic brain injury, and 4 cases (0.3%) of other causes such as cerebral edema and brain lesions. There were 51 foreign donors for whom the necessity of autopsy was discussed, and 29 patients were subjected to autopsy after donation by judicial judgment, and 22 patients were donated without an autopsy. Of these, 22 donations were made through 15 supplementary investigations and 7 direct autopsies through visits to the prosecutor’s office. The 51 deaths were 33 suspected crimes, 11 falls, 2 traffic accidents, 2 fire accidents, and 2 medical accidents. There was one case of asphyxiation from gas during operation.

Conclusion: From 2016 to 2021, 49.4% of brain death donors were foreigners, and patients with the need for autopsy among foreigners will continue to occur. Accordingly, it is necessary to find ways not to restrict "judicial procedures" and "brain death donation". It is believed that the role of the organ acquisition agency is to reflect the intention of the family who decided to donate through sharing cases that could be donated without interfering with the exact cause of death, such as initial intervention by forensic experts, conditional approval according to circumstances, and observation of donation surgery.

P11.21
Appointed Donor Responsible Doctor and Donor Responsible Nurse Increase Organ Transplantation in Sweden

Wenche Stribolt1, Camilla Olofsson1, Helena Almen1.

Introduction: To follow up the quality and efficacy of the organ donation process, and subsequently to increase organ transplantation in Sweden, the National board of Health and Welfare uses five quality indicators, Donor Responsible Doctor (DRD) and Donor Responsible Nurse (DRN) have a key role in promoting donation and supporting the quality assurance of the donation process in the ICU. The appointment of DRD and DRN is one of the indicators. This abstract focuses on the development of appointed DRD and DRN between the years 2016-2021, thus including the unprecedented covid-19 year of 2020. Donors in numbers are also presented.

Method: According to the national target value, 100 % of the intensive care units (ICUs) should have appointed DRD and DRN with written assignment description and the recommended time for the assignment (2-8 hours/week depending on the type of ICU). Appointed DRD and DRN is reported by the health care professionals into the Swedish Intensive Care Registry (SIR) since 2016. Data for 2021 is not available at the time of submission, but will be available at the conference. The number of utilized donors for the years 2016-2021 is retrieved from Scandiatransplant. Descriptive statistics, proportion of appointed DRD and DRN and number of utilized donors, are presented.

Results: The appointed DRD and DRN were as followed in 2016; 38% and 47%, 2017; 40% and 48%, 2018; 33% and 41%, 2019; 39% and 45%, 2020, 52 % and 55 % (those ICUs not reporting are not included in the calculations). Although the proportion of DRD and DRN has increased from 2016 to 2020 it is far from the set goal of 100%. Those ICUs not reporting DRD and DRN were in 2016; 26%, 2017; 14%, 2018; 14%, 2019; 9%, 2020; 25% (combined for DRD and DRN). The results for 2021 will be presented at the conference. The number of utilized donors were in 2016; 185, 2017; 188, 2018; 182, 2019; 191, 2020; 174, 2021; 192.

Discussion: DRD and DRN have a key role in promoting organ donation. The reasons for the high number of ICUs not reporting appointed DRD and DRN (25%) during the covid-19 pandemic year 2020 compared to previous years is not known. It could be explained by a displacement effect due to the pandemic. Either were the DRD and DRN not appointed, or there was simply a lack of time to report to SIR. Although the number of donors dropped from 191 in 2019 to 174 in 2020, one could have expected a greater decrease due to the pandemic. Also, in 2021 the number of utilized donors reached 192. These results indicate that, despite the strain caused by the pandemic, the ICUs managed to identify donors. The indicators DRD and DRN has to be reviewed in depth, and be correlated to the numbers of donors within each region of Sweden.

Conclusion: The main findings show that DRD and DRN are not being appointed as required by the Swedish regulations, or not being reported to SIR as should. As the number of utilized donors increased in 2021, the negative effects of the pandemic were limited.
**P11.24**

**The Korean Experiences of Re-Use Transplanted Liver Or Kidney: Case Series**

Eun Jin Woo1, Youn Jung Choi1, Minhwa Kim1, Hye Young Kim1, Yang Suk Pak1, Jeongrim Lee1, Insung Moon1, Byunghyun Choi2, Taehee Kim2.

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**Introduction:** Because of chronic shortage of organ, the re-use of transplanted organ may be a good option for urgent recipients. However, the reports about re-use of transplanted organ are relatively rare worldwide. We would like to share the experiences of re-use transplanted organs in Korea.

**Case review:**

- **Liver:** Among the six recipients of re-use grafts, three of them were successfully recovered. However the other three transplants were going to graft failure. The cause of high graft failure rate could be the two ischemic attacks in relatively short period. The last case was successfully transplanted after more than five years from the first liver transplant. So there was no second ischemic damage in the graft. The graft biopsies or laboratory findings (AST, ALT, Total bilirubin, INR) performed during the transplant had no predictive value of graft failure.

- **Kidney:** The two of three recipients were successfully transplanted and their kidney have been well-functioning more than seven without adverse event. 1 recipient had transplanted re-used kidney successfully, but graftectomy was required because of bacterial infection before discharge.

**Conclusions:** The transplantation of previous transplanted organs could be possible in the urgent situation. However, the ischemic damage should be carefully considered in liver transplant cases. In the case of kidneys, even if transplanted organs are reused, the retal function is maintained well. But we need to understand and recognize the risk of infection.

**P11.25**

**Why Do Not All Living Kidney Donor Candidates Are Accepted For Donation? A Pediatric Center Experience**

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**Introduction:** Living donor kidney transplantation is the best type of renal replacement therapy for patients with end-stage renal disease, providing numerous clinical benefits when compared with prolonged dialysis or deceased donor kidney transplantation. These include longer patient and graft survival, decreased waiting period on the transplantation list and improved quality of life. Living kidney donors (LKDs) go through an extensive evaluation to ensure the safety before proceeding for donation, and many potential LKDs are declined because of different reasons. The aim of this study was to define the reasons for declining potential LKDs referred to our center.

**Methods:** We retrospectively analyzed clinical data of all potential LKDs evaluated between January 2001 and December 2021, at our institution CMNO, Pediatric Hospital. Data were obtained by review of an electronic database. Data for quantitative variables were presented as mean, standard deviation and range, and categorical variables as frequencies and percentages.

**Results:** A total of 1332 potential LKDs were evaluated, 796 (59.7%) successfully donated, 20 (1.5%) has a complete evaluation, accepted for donation and in waiting list for intervention, 56 (4.2%) continues in evaluation process, 200 (15%) were discharge from the program due to administrative reasons, death (donor or receptor) or cadaveric renal transplantation in order of frequency, 56 (4.2%) withdraw by personal choice at variable time points during the evaluation process, and 204 (15.3%) were rejected for donation.

Donor-related reasons included medical contraindications (n=134, 65.7%), anatomical contraindications (n=38, 18.6%), immunological barriers (n=18, 8.8%), and psychological reasons (n=11, 5.4%).

**Conclusions:** Despite the large number of potential LKDs a significant proportion do not proceed for donation at some point during the evaluation process, in our description, it represents 40.3%, a total of 536 patients that keep waiting for a kidney transplant. Most of the reasons are consequence of candidate’s medical conditions, standing out the prevalence in our population of unnoticed chronic diseases (obesity, diabetes mellitus, impaired glucose tolerance, hypertension) and its impact on kidney function. Since the deceased donor pool is limited and provides fewer benefits, modifying accepting criteria such as accepting potential LKDs with mild obesity or well-controlled hypertension might be needed. These numbers highlight the need for increased public awareness of living donation, more careful but inclusive screening, targeted educational programs, and ongoing support for potential LKDs.
Abstracts P11.26

Serological Profile of Donors in Argentina

Marisa Cobos, Gabriela Hidalgo, Carlos Soratti.

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Abstracts S679

Introduction: The serological profile of donors is the beginning of the infectological traceability of the donation and transplant process. Complementary studies are positioned as a transcendent source of information, along with clinical examination, especially when the history of donors is unknown. The knowledge of these data allows us to implement various strategies aimed at the quality of care of the recipients and on the other hand allows us to carry out an epidemiological surveillance of the microorganisms prevalent in the different regions of our country. We present the serological profile of donors in Argentina during the period 2017-2021.

Methodology: Descriptive and retrospective study. The donation processes initiated during the period 2017-2021, registered in SINTRA, were selected. The presence of complete serological studies was considered as an inclusion criterion. The serological memory variables for viruses (HIV, HTLV, CMV, HBV, HCV), bacteria (Treponema pallidum, genus Brucella) and parasites (Trypanosoma cruzi, Toxoplasma gondii) of donors in Argentina during the period were analyzed.

Results: The processes initiated in the period 2017-2021 were 18,242. The processes that documented complete serological studies were 5,889. 85.3% of the donors, during the period analyzed, were from 9 jurisdictions (Buenos Aires, CABA, Santa Fe, Córdoba, Mendoza, Tucumán, Misiones, Entre Ríos and Santiago del Estero). 14.7% corresponds to the rest of the country. From the serological analysis of the donors of the 9 jurisdictions mentioned, cytomegalovirus (89.7%) and Toxoplasma gondii (45.15%) were observed as prevalent serology. We identified 0.31% of reactive serologies for HIV, 0.23% for HTLV, 0.95% for HCV and 2.74% for Treponema pallidum. In reference to hepatitis B markers, 1.47% of donors presented isolated Ac HBc, the Ac HBc + Ag HBs association was observed in 0.13% and the Ac HBc + Ac HBs association in 2.2%. 1.07% of donors were reactive for Huddleson reaction. 2.94% presented at least 2 reactive serologies for Chagas disease.

Conclusions: The epidemiological surveillance of donors makes it possible to consider possible modifications in the infectological recommendations of the selection of the donor and the follow-up of the recipient.

S679
Changes in Markers of Coagulation and Fibrinolysis Offer Insights Into Pathophysiological Aspects of Preservation Injury During Normothermic Liver Perfusion

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¹Department of General Surgery, Division of Transplantation, Medical University of Vienna, Vienna, Austria; ²Department of General Surgery, Medical University of Vienna, Vienna, Austria

Background: The perfusate used in normothermic machine perfusion (NMP) is mainly composed of red packed blood cells and colloid solution and is therefore free from thrombocytes and coagulation factors. Our aim was to monitor changes in composition of coagulation factors during NMP and to investigate their association with liver function during NMP and after transplantation.

Methods: NMP has been performed on a heterogenous study group of 16 grafts that included 12 extended criteria donor livers. Factor V activity (FV), factor XIII activity (FXIII), van Willebrand factor activity (vWF), D-dimer, plasminogen-activator-inhibitor (PAI-1) and thrombocyte count in perfusate were assessed. Liver and bile duct biopsies were taken before and after perfusion and after reperfusion. Median follow-up after transplantation was 11 months (IQR: 6.4-12).

Results: NMP and assessment of 16 livers resulted in 10 livers that were successfully transplanted. Main reasons for decline included inability to clear lactate, low bile quality, or signs of fibrosis in the frozen section. Two livers were successfully transplanted. Main reasons for decline included inability to clear NMP included increased D-dimer levels during perfusion (8.7 µg/mL and 12.3 µg/mL vs. mean peak D-dimer of 3.7 µg/mL SD: 3.1). One liver was transplanted, the histological analysis of the bile duct biopsies taken before implantation showed sclerosing cholangitis. Additionally, vWF activity during perfusion of this liver was increased (15 % vs. mean peak vWF activity of 6.4 % SD: 2.5). The recipient had to be treated with a stent for an anastomotic stricture. The second liver with elevated D-dimer was severely steatotic and the only liver out of the study group that did not produce bile and was therefore declined for transplantation. The graft additionally presented with increased D-dimer levels during perfusion (8.7 µg/mL and 12.3 µg/mL vs. mean peak D-dimer of 3.7 µg/mL SD: 3.1). One liver was transplanted, the histological analysis of the bile duct biopsies taken before implantation showed sclerosing cholangitis. Additionally, vWF activity during perfusion of this liver was increased (15 % vs. mean peak vWF activity of 6.4 % SD: 2.5). The recipient had to be treated with a stent for an anastomotic stricture. The second liver with elevated D-dimer was severely steatotic and the only liver out of the study group that did not produce bile and was therefore declined for transplantation. The graft additionally presented with high levels of PAI-1 (299 IU/mL vs. mean peak PAI-1 of 186 IU/mL SD: 155) and increased FXIII activity in perfusate (158 % vs. mean peak FXIII activity 45% SD: 49). PAI-1 was also elevated in another three livers during perfusion, of which one was discarded due to increasing lactate after initial clearing and high grade of steatosis (peak PAI-1 605 IU/mL). Both other livers were successfully transplanted, one of the two recipients later developed an anastomotic stricture. Each of the three cases with increased PAI-1 levels coincided with peaks in either thrombocyte count, bilirubin or FV activity.

Conclusion: Changes in perfusate composition of coagulation and fibrinolysis factors offer interesting new insights in pathophysiological aspects of preservation injury and might allow for additional graft assessment during longer courses of NMP. Prospective studies are needed to validate these initial findings.

Effect of Temporal Trends in Donor Demographics on Perioperative Outcomes in Robotic Living Donor Nephrectomy

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Introduction: Due to the advantages of robotics over conventional laparoscopy, Robotic living donor nephrectomy (RLDN) is increasingly being adopted for kidney harvest. This study was undertaken to determine the effects of temporal trends in donor demographics on perioperative outcomes in RLDN.

Methods: All living donors who underwent RLDN from March 2000 to March 2013 at the University of Illinois, Chicago, were included in this single-center retrospective study. The patient demographic and clinical characteristics were recorded. The focus of the study was perioperative surgical outcomes in terms of operative time (ORT), warm ischemia time (WIT), estimated blood loss (EBL), length of stay (LOS), complications, and readmission rate. The consecutive LDs (Living donors) were divided chronologically into four different groups corresponding to the four different epochs in time to assess the refinements in the surgical technique on the outcomes of RLDN. The clinical and surgical outcome variables were compared temporally statistically examined, and inferences were drawn. All analysis was carried out using SAS 9.3 (SAS Institute, Cary, North Carolina, USA).

Results: A total of 800 consecutive donors underwent robotic-assisted donor nephrectomy. The mean donor age was 36±11.0 years, and there were more females than males. The BMI varied from 17-53kg/m2 with a mean BMI of 29.2±5.7 Kg/m2, and 62.6% of donors were first degree relatives of the recipients. The proportion of left kidneys procured was 95.7%. Arterial anomalies were present in 26.1% of donors, while 2, 3, and 4 arteries were present in 22.4%, 2.3%, and 0.2%, respectively. Venous anomalies were present in 16 patients overall. Most procedures (98.8%) were conducted with robotic assistance. Five cases (0.6%) were converted to an open, while another 4 patients had another concurrent procedure during the robotic nephrectomy, as shown in table 1. From the year 2000 to 2013, a gradual increase in donor age was observed (p=0.01) (Table 2). There were no changes in the male to female ratio and the mean BMI temporally. Donations across all races increased significantly (p<0.0001) except Hispanics. Statistically significant increases were noted in ORT (p<0.0001), WIT (p<0.0001), EBL (p<0.0001), and LOS (p<0.0010) between the last and previous era, as the new surgeons and fellows took over as console surgeons. Although the complication rates significantly decreased from 2000-2013 (p<0.0001), there has been a steady increase in readmission rate over time (p<0.0001), as shown in the table below (Table 2).

Conclusions: The results from this study reveal that RLDN is a safe technique that can be used for safe kidney harvest across a different subset of patients with a wide range of BMI. In addition, the method is safe despite new surgeons and fellows being introduced as console surgeons.
Improving Tissue Donation Referral Rates From the Emergency Department - A QI Project

Susan Macmillan, 1
1 Emergency Department, NHS Forth Valley, Larbert, United Kingdom

Abstract

P11.29

Improving Tissue Donation Referral Rates From the Emergency Department - A QI Project

Susan Macmillan 1
1 Emergency Department, NHS Forth Valley, Larbert, United Kingdom

Background: This project was undertaken by a Junior Dr a hospital Emergency Department (ED) in Scotland. The aim was to increase tissue donation referral rates for deceased patients, by referring at least 50% of potential donors. Eligible potential donors were those who did not have dementia, haematological malignancy or blood borne virus. The number of potential donor deaths monthly was around 7, making tissue referrals a low frequency but high acuity event. It was a small project but so successful that the materials developed were rolled out Nationally.

Method: Using the Plan Do Study Act approach, multiple departmental interventions were undertaken. These included surveying staff to identify barriers to tissue donation; focused teaching moments; posters to prompt staff in key clinical areas; development of a clear process algorithm, pocket sized laminated Tissue Donation Information cards for staff, as well as a suggested “script” to raise donation with families, and regular progress updates on referral rates both written and verbal. The Potential Donor Audit data was collected monthly from August 2017 until June 2019 by the Tissue Donor Co-coordinator on all deaths and referrals from the department. Prior to this there had been no referrals made. Before approaching families to discuss tissue donation the Tissue Donor Co-coordinator should be contacted to check the Organ Donor Register and confirm eligibility for donation. This is considered as a ‘referral’ for audit purposes irrespective of whether donation proceeds.

Results:

□ The aim of referring 50% of eligible potential tissue donors to the tissue donor co-coordinator was achieved during the data collection period (average 55%).
□ The project commenced in August 2017 and data was collected until June 2019.
□ The interventions implemented are outlined in the table and correspond to the arrows on the chart.
□ Anecdotal feedback from staff involved has demonstrated many families took comfort from donation and staff felt more comfortable approaching families using the suggested wording.
□ In total, 2 hearts (for valve donation) and 26 eyes (for corneal donation) were donated by patients. Two further hearts were accepted for donation but unable to be retrieved due to operational reasons.

Conclusion: This project resulted in significant improvement in referral rates. The cumulative effects of the interventions are most likely to have resulted in the improvement. Anecdotally staff feed back that the process flow chart and the pocket information cards have been the most helpful interventions in their day to day practice. The methods used in this Quality Improvement Project could readily be applied in other ED’s who are introducing tissue donation or looking to improve referral rates. During 2021 the prompt cards developed were disseminated Nationally to ED’s and Intensive Care Units in Scotland who are able to facilitate Tissue Donation.

Table 1: Demographic and clinical characteristics of living donors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>No. of patients (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean +/− SD</td>
<td>36.0±11.0</td>
<td>800</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td>800</td>
</tr>
<tr>
<td>Male</td>
<td>378 (47.2%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>422 (52.7%)</td>
<td></td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td>800</td>
</tr>
<tr>
<td>White</td>
<td>190 (23.7%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>302 (37.7%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>257 (32.2%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>51 (6.3%)</td>
<td></td>
</tr>
<tr>
<td>Donor-recipient relation, n (%)</td>
<td></td>
<td>800</td>
</tr>
<tr>
<td>First-degree relative</td>
<td>501 (62.6%)</td>
<td></td>
</tr>
<tr>
<td>Second-degree relative</td>
<td>71 (8.8%)</td>
<td></td>
</tr>
<tr>
<td>Unrelated</td>
<td>228 (28.5%)</td>
<td></td>
</tr>
<tr>
<td>Anthropometric measurements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (Kg), mean +/− SD</td>
<td>83.3±18.3</td>
<td>792</td>
</tr>
<tr>
<td>Height (cm), mean +/− SD</td>
<td>168.6±10.3</td>
<td>707</td>
</tr>
<tr>
<td>BMI (Kg/m²), mean +/− SD</td>
<td>29.2±5.7</td>
<td>708</td>
</tr>
<tr>
<td>Pre donation BP and Labs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre donation DBP (mmHg), mean +/− SD</td>
<td>73.8±10.1</td>
<td>800</td>
</tr>
<tr>
<td>Pre donation Creatinine (mg/dl), mean +/− SD</td>
<td>0.8±0.1</td>
<td>770</td>
</tr>
<tr>
<td>Pre donation Blood glucose (mmol), mean +/− SD</td>
<td>90±12</td>
<td>800</td>
</tr>
<tr>
<td>Anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latent risk of diabetic kidney, n (%)</td>
<td>798</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>764 (95.7%)</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>34 (4.2%)</td>
<td></td>
</tr>
<tr>
<td>Vascular anomalies, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial anomalies</td>
<td>200 (26.4%)</td>
<td>707</td>
</tr>
<tr>
<td>Venous anomalies</td>
<td>16 (2.1%)</td>
<td>705</td>
</tr>
<tr>
<td>Both Arterial and venous</td>
<td>8 (1.0%)</td>
<td>707</td>
</tr>
<tr>
<td>Number of arteries, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>597 (74.9%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>179 (22.8%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>19 (2.5%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2 (0.2%)</td>
<td></td>
</tr>
<tr>
<td>Number of veins, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>779 (97.9%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>15 (1.8%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 (0.1%)</td>
<td></td>
</tr>
<tr>
<td>Number of ureters, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>746 (99.4%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4 (0.1%)</td>
<td></td>
</tr>
</tbody>
</table>

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Abstracts

S681
**Tissue Donation**

3 to 95 years old

**Absolute contra-indications:**
- Blood borne viruses
- Haematological malignancy
- Dementia

**NB:** Patients over 70yrs cancel donation only

**Tissue Donor Co-ordinator** 07623 513 987 24 hours

---

**Intervention Key:**

1. Tissue donation information screen saver on all ED PC’s (sept 2017)
2. Small leaflet prompt for all staff (Sept 2017)
3. Reminders in morning handover meetings for clinical staff for one week and then monthly (Sept 2017)
4. Prompt slip attached to death checklist (Oct 2017)
5. Resus Poster (Nov 2017)
6. Potential Donor Audit results to be discussed in monthly consultant M&M (Nov 2017)
7. Development of clear process flow chart (Dec 2017)
8. Formal teaching to junior doctors (Dec 2017)
9. Focused 5 min teaching sessions with Dr’s and Nurses (from Jan 2018)
10. Revised process flow chart with suggested wording (Jan 2018)
11. Pilot of laminated pocket information “Prompt cards” for doctors nurses (Feb/March 2018)
12. Final version of Prompt Cards (figure 4) alongside “Tissue Donation Week” awareness raising event (Feb 2019).

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**Step by step process in Tissue Donation folder - Resus Bay 1**

**Suggested discussion...**

“In these circumstances we routinely check the Organ Donor Register. Your loved one was/was not on the Donor Register. There may be the opportunity to donate tissues like corneas to improve the lives of other patients. Donating tissues shouldn’t cause delays to funeral arrangements or affect viewings. You don’t have to decide now. Would you like us to arrange for the Tissue Donor Co-ordinator to call you to discuss it?”

---

**Figure 5:** % potential donors considered for tissue donation

<table>
<thead>
<tr>
<th>Date</th>
<th>% Potential Donors Considered</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/1/2020</td>
<td>12.2%</td>
</tr>
<tr>
<td>5/1/2020</td>
<td>9.6%</td>
</tr>
<tr>
<td>6/1/2020</td>
<td>13.9%</td>
</tr>
<tr>
<td>7/1/2020</td>
<td>4.7%</td>
</tr>
<tr>
<td>8/1/2020</td>
<td>21.1%</td>
</tr>
<tr>
<td>9/1/2020</td>
<td>12.3%</td>
</tr>
</tbody>
</table>

The arrows indicate the timeframe of interventions as listed in figure.
P11.30

Influence of Basic Cardiopulmonary Reanimation on Uncontrolled Donors After Cardiac Death

Alonso Mateos-Rodriguez1,2,3, Maria Jose Polonio Anguas1, Maria Cristina De La Torre Toyos1, Jose Maria Navalspoto Pascua2, Carmen Cardos Alonso3, Fernando Neira Serrano2, Francisco Jose Del Rio Gallegos1.

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Introduction: The objective of this study is to determine if the application of basic CPR in patients who have undergone a CPA and, subsequently, have been referred as donors in uncontrolled asystole, has any influence on the procurement of organs for transplantation.

Material and Methods: The variables collected are affiliation data, performance of bCPR, cause of death, attendance times and donated organs. The analysis with quantitative variables that follow normal distribution, are shown as mean ± SD and student’s t test is applied to compare. The analysis of the variables that do not follow the normal distribution are shown as median [interquartile range] and the Wilcoxon test is applied to compare.

Results: 91 cases of transfers of possible DANC are collected. bCPR was performed in 61 patients (67.7%) and bCPR was not performed in 27 patients (23.3%). Of the group that received bPCR, 39 (73.6%) patients were ultimately effective donors compared to the non-bPCR group in which 22 (62.9%) were effective donors (p=0.28).

Conclusion: According to our series, performing basic CPR does not seem to increase the chances that this patient will be a donor. Not even doing a detailed analysis by donated organ (kidney, liver or lung) we were able to detect an association with bCPR.

P11.31

Gendering Organ Donation: Experiences of Living Women Organ Donors in India

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Introduction: Living organ donation is the predominant method to obtain organs for transplant in India due to increasing cases of organ failure and limited cadaver organ donations. The data from National Organ and Tissue Transplant Organisation (NOTTO) for 2019 revealed that 78% of living organ donors are women. The proportion between receiving and donating organs reflects the existing gender and sex-based disparity. This inequality proves unfavorable towards women, and women constitute most of the living organ donors in India. The lack of research on living organ donors in the Indian context undermines the evidence on prevalent gender disparity in organ donation. Thus, this study aims to explore the experiences of women living organ donors to understand the reasons, decision-making process, and their experiences with the health care system during the donation process.

Methods: A qualitative exploratory design was employed to understand the experiences of living women organ donors. Fifteen in-depth interviews were conducted between May to July 2017 with women in Rajasthan (India), using Snowball sampling. The interviews were transcribed, translated, and analyzed using thematic analysis. A critical gender perspective was applied to elicit the role of patriarchy and gender roles during the data collection and analysis stage.

Results: Of the women interviewed, ten women had donated an organ to their spouse, and five had donated to their children. Women donors expressed a sense of self-sacrifice and a greater responsibility towards the health and wellbeing of the children and spouse. They perceived organ donation as their maternal or spousal duty to reduce the suffering of their husband/child and save their life. When encouraged or urged to donate their organs, women did not resist because they considered it their responsibility. During the organ donation process, male family members took charge of all documentation, whereas women only signed the documents. Women donors have not explained the organ donation process or the future health risks associated with the procedure. In most cases, doctors assured them that they would have a healthy life after donation; however, they experienced discrimination and neglect towards their health after the procedure from family and the health staff.

Conclusion: The study provides the empirical ground of women’s over-involvement as a donor which unveils the existing gender disparity and an unseen pressure on them being a wife or a mother to the recipient. In patriarchal societies like India, gender roles and existing power dynamics force women to become organ donors. Further, women’s right to health and autonomy over their bodies is compromised during organ donation.
P11.32

Brain Death in Uruguay: 19 Years of Experience

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Objective: Describe the Epidemiology of Brain Death (BD) in 19 years.

Material and methods: We studied potential donors reported to the National Registry of Donors diagnosed with BD between 2002 and 2020. We analyzed: total number of communications, age distribution, causes of death, BD diagnostic method, medical contraindications, family refusals, real donors and conversion of BD to real donor.

Results: They communicated 2770 BD from all over the country, the age distribution was mainly between 18 and 60 years old, representing 70%. In extreme ages we had the lowest percentage of diagnoses with 2.2% between 1 and 5 years and 2% in those older than 75 years. Taking globally those over 65 years of age, these were 10.1% of BD. There were no differences regarding the months of the year or the days of the week in which the BD were reported. The time of greatest communication was between 1:00 and 6:00 p.m., 36% and from 7:00 to 11:00 p.m. 23%. Causes of death: CVA 51.1% followed by TEC with 23.4%. The diagnosis of BD was clinical and Doppler was used in 20%. Doppler was used as an auxiliary method in 6.8% in 2019 and 9.2% in 2020. The medical contraindications were: sepsis 16%, poor hemodynamics 10.8%, tumor 12%, hypertension/diabetes 16%. The family refusal prior to the implementation of the presumed consent law was 54.4% and of the total communications of BD that had prior expression of donation in the National Registry of Donors, 46.7% were negative. The real donors in this period were 1125. Conversion from BD to Real Donor of 40%. Analyzing the conversion in the years following the implementation of presumed consent, the average conversion was 51.6% 860BD/444 DR, DR over 65 years old were 5.4%, 66 to 70 years old 4.1%, 71 to 75 years old 1.1% and over 75 years old 0.08%.

Conclusion: Uruguay has a rich experience in donation and transplants. This analysis of 19 years of BD communications leaves some important conclusions: a decrease in BD in children under 5 years of age, low use of people over 65 years of age as real donors, and a clear benefit of the presumed consent law over the refusal to The donation.

P11.33

Donation and Transplantation Indicators in the Pre and Post Pandemic Stage. Tasa Use

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Introduction: The donation indicators decreased due to the pandemic in 2020. The redirection of resources and the uncertainty generated during the first stages are some of the reasons. Preserving this activity, even in a pandemic, is a need and an obligation.

Objective: Evaluate the impact of the pandemic on the rate of use of solid organs in Latin America.

Methods: Population of donors in Latin American countries was analyzed in a descriptive observational study. The data was extracted from the donation and transplant registry published in the Newsletter 2021. For this analysis, the rates of global and specific cadaveric donors for each organ (including liver, heart and lung) expressed as pmp donors were considered. The rate of use was calculated as: a ratio of the actual transplant, rate to the expected transplant, rate based on the donor rate pmp (assuming multi-organ cadaveric donors).

Results: The average Latin American donation rate was 11.7 pmp in 2019 and 7.3 pmp in 2020. The usage rate of liver was 49.8%, heart 16.5% and lung 5.5% in 2019. The usage rate for liver was 60.8 %, heart 18.2 %, and lung 6.24 % in 2020. Central America: donor rate pmp 5.76 in 2019 and 2.4 pmp in 2020. The liver usage rate was 36.2 % in 2019 and 31.4% in 2020. Conclusions: A decrease in the pmp donor rate was observed in 2020 linked to the pandemic, but the rate of use was higher in the three organs in Latin America. There was better use of donors. Could we maintain or improve the efficiency of the procedures and thus increase the donation rates in these organs? In Central America and the Caribbean, this better use was not observed. The low number of countries may bias this result.
P11.34

Tissue Donation Indicators in Latin American and European Countries. A Way to Measure the Efficiency of the Organizational System

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Introduction: The demand for corneas is increasing in the world. Organizational aspects of the health system and procurement are decisive to improve the number of corneal donors. There are no corneal donation indicators at the international level that allow results to be compared other than the total number and donation rate.

Objectives: Analyze the corneal donation situation worldwide, defining indicators related to the deceased in the country. Compare the donation indicators defined in countries of both continents: Latin America and Europe.

Material and methods: The following data in Latin America and Europe were analyzed: number of corneal donors/pmp (Dc/ pmp), number of organ donors/pmp (DO/ pmp), corneal donors in PCR/ pmp, and total number of deceased from the country. The relationship between the total number of corneal donors in each country and the number of deaths in 2019, grouped by continent, was analyzed. Indicator: Corneal donors/Deceased in the country.

The relationship between the number of corneal donors in PCR and the total number of corneal donors of all countries grouped by continent was also analyzed. Indicator: Corneal donors in PCR/total corneal donors. The data was obtained from the Newsletter Transplant 2019 and the number of deceased at https://ourworldindata.org/.

Results: In Latin America, the average number of Corneal donors/deceases per country is 0.51%, with Brazil being the most efficient with 2.1%. In Europe, the average number of Cornea donors/deceased is 0.48%, where Italy, France and the Netherlands stand out with 1%, 1.4% and 1.3%. In the Latin American countries analyzed, the average number of Cornea donors in PCR/ total cornea donors is 69% and in European countries it is 59%.

Conclusions: We believe that the indicator Corneal donors/deceased in a country or hospital is a strong indicator that can be used to define the effectiveness of corneal procurement work and compare results in different countries. Analyzing the percentage of donors of corneas in PCR, we can evaluate the work as a country in the procurement of this tissue in PCR to improve the organizational level in the detection of donors of PCR.

P11.35

Using Emotional Text Mining to Explore the Cultural Representation of Organ Donation in the Spanish and Italian Culture

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Introduction: Spain is considered the world leader in the field of organ donation, reaching the highest percentage of donors. This is the effect of an organization based on strong network relationships, specific training for health professionals and a focus on the promotion of organ donation among the population. Other countries, such as Italy, have adopted the Spanish model in their healthcare model for this issue, but still failing to reach the Spanish primacy. Cultural representation of organ donation can variate among countries, explaining the differences in the number of final donors. In literature there are no research on this facet of organ donation. With this work we aimed to investigate the cultural elements influencing the choice to donate in Italy and Spain.

Method: To achieve this goal, we collected from two of the major newspapers of Italy (Il Corriere della Sera and La Repubblica) and Spain (El País and El Mundo) all the published articles between 2001 and 2021, containing the respective translation of “Organ Donation”. The two large final corpus, made up of 846 articles for the Italian and 571 for the Spanish one, were analyzed through the Emotional Text Mining (ETM; Greco & Polli, 2020), a non-supervised text mining methodology that allows the detection of cultural representations that sets people interactions, behaviors, attitudes, and communication.

Results: The analysis produced 4 cultural representations for the Italian corpus and 5 cultural representations for the Spanish one. The principal representation for Spain is the organ donation as a national project, while in Italy prevails the facet of donation as a saving-life product, more oriented to an individual point of view. In Italian newspapers emerges the theme of death, an element felt as necessary as unacceptable. In Spain the principal step for donation is the family where citizens, as potential donor, can discuss about donation. Moreover, donation has a point of view on the circle of life, where death is a step to a final vision of lifesaving. Another big difference between the two nations is related to developmental process: the Italian model seems to be rooted in established promotional models, while in Spain emerges the desire for continuous growth and innovation, founding the promotion of organ donation on a strict relation between the citizen and the State. Finally, in Spain organ donation is connected to other fields (e.g. blood, gamete and tissue donation), while in Italy the issue is lived as totally isolated from other context.

Conclusion: In conclusion, exploring the cultural representations of organ donation in these two countries allowed us to understand deep cultural differences. Results would be used for countries to work on the sensible areas, such as with focused promotional campaigns to the citizens. This work could help to improve the substantial differences in donation rates, increasing in this case the number of Italian donors.
**P11.36**

**Indocyanine Green (ICG) Angiography for Assessing Microcirculation Patency Improvement After Hypothermic Machine Perfusion (HMP) Re-Conditioning: A Pilot Study**

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**Background:** Nowadays, given the widening gap between organs available and patients on dialysis waitlisted for kidney transplantation, many efforts are steered to expand the donor pool. Resorting consistently to marginal organs, clinical, instrumental and histological methods, that will be specific and accurate in assessing the quality of the graft before transplantation, might be advisable in order to prevent any complications, helping to state if the graft has to be transplanted as a single or dual kidney or discarded. Our aim is to test indocyanine green angiography for the assessment of microcirculation patency improvement after Hypothermic Perfusion Machine (HMP) re-conditioning in order to contribute to defining graft quality, jointly with pretransplant biopsy findings and renal resistive index assessed at the end of hypothermic perfusion.

**Methods:** We conducted a prospective cohort study performing indocyanine green fluorescent angiography during back table surgery before and after hypothermic perfusion on all kidneys available for transplantation which required the treatment because retrieved from Extended Criteria Donors (ECDs) or Donors After Cardiac death (DCDs).

**Results:** From June 2020 to July 2021 we enrolled 5 grafts retrieved from DCDs selected for transplant and treated through HMP. All perfused kidneys showed a significant rise in terms of fluorescence intensity after HMP treatment: four out of five closes to doubling. Furthermore, statistical analysis demonstrated a moderate correlation (r = 0.3972798889383) between fluorescence intensity with the final resistance index scanned at the end of HMP treatment.

**Conclusions:** Our results establish how fluorescence can be a valid and cost-effective method for evaluating the graft before transplantation, jointly with histology and renal resistive index assessment. Further studies are needed to standardize this technique.

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**P11.37**

**A New Successful Training Method for Brain Death Family Approach**

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**Introduction:** The capability of organ donation coordinators (ODCs) is very critical in getting the family’s consent for organ donation. So, improving this skill in them is a very important matter. One way to improve the success of ODCs in brain death family consent is holding training courses for them. Iranian Family Approach Specific Course (IrFASC) is a novel and unique training method for ODCs. The aim of IrFASC is improving the knowledge level, increasing confidence, and preparing ODCs for in approaching the brain death families. This study’s aim is to investigate the effects of IrFASC on ODC’s ability and their success in the family consent process.

**Methods:** Due to the COVID-19 pandemic, a new virtual training course, IrFASC, was designed. This 60-hour training course (5 days long) contained 22 topics on methods of brain death family’s approach. In this course, different sections were designed to increase the impact of the training, consisting of: project-based learning, thinking-based learning, discussion-based learning, brain-storm learning, problem solving, and simulation. IrFASC was held for 3 groups. The first group training course was performed 12 months ago, the second group six months ago and another one three months ago. The success rate of participants in the same intervals (12 months for group 1, six months for group 2, and 3 months for group3) was measured before and after the training course. The success rate of coordinators before and after the training course was compared using the dependent sample t-test.

**Results:** Thirty volunteers participated in three separate groups in training courses. From them, 11 participants were male. The median confrontation with the family of patient with brain death was 5.5 times (min:2 and max:35) before the training course and 8 times (min:2 and max:40) after the training course. Overall, the training course improved the rate of coordinators’ success (increasing the rate of success from 53.04 to 65.26%, p value=0.003) (table 1). Sub-analysis on groups showed that this improvement is more significant in long periods and the percent of success increased 19.39% in group 1, 8.03% in group 2, and 15.20% in group 3. Furthermore, sub-analysis on coordinators’ gender showed that female coordinators’ improvement was significant during training course (p value=0.02) but this increase was not significant in males (P value=0.06, Table2).

**Conclusion:** Considering the impact of IrFASC course on improving ODCs’ performance, holding this course for other coordinators is also recommended.

| Table 1. Rate of coordinators successful before and after training course |
|-----------------------------|------------------|-----------------|-----|
| Groups               | The rate of success before the training | The rate of success after the training | P value |
| All (n=30)            | 53.04            | 65.26           | 0.003 |
| Group 1 (12-month, n=6) | 47.55           | 66.95           | 0.022 |
| Group 2 (6-month, n=16) | 52.87           | 60.91           | 0.170 |
| Group 3 (3-month, n=8) | 57.50           | 72.70           | 0.091 |
Impact of Two Different TV Content on Promote Organ Donor Registration

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Introduction: The most important limitation of organ transplantation is the shortage of available organs for transplantation and taking action on raising awareness in society about this issue may be helpful. The aim of this study is to investigate the impact of media on organ donor (OD) registration in Iranian population. Furthermore, this study compares the effectiveness of two different type of media program (OD documentary TV program and short inspiratory messages during soccer events) on OD registration.

Method: The present community-based intervention study starts from September 1st to the end of November of 2018. Two different media content were used to increase awareness of people towards OD. The first media program was an OD documentary TV program and the second was through short inspiratory messages delivered to people (Television spectators) during soccer events. The documentary was designed as a 12-episode series, focused on the humanitarian benefits of donation and the overall process in Iran. Each episode lasted 1 hours. The episodes were broadcasted weekly. Each episode was focused on a separate organ recipient and different processes relevant to organ donation was explained accordingly. The short inspiratory messages such as subtitle were delivered before, after and during half-time of 10 separate soccer matches that were held during the time-frame of the present study. The soccer host further emphasized the delivered messages during the half-time and after the game, during the after-game interpretations.

Results: The mine characteristics of registered persons in September, October, and December is provided in the table 1. Analysis showed that the media campaign had a significant effect on encouraging people to get OD card (P<0.001). There is significant different between documentary and soccer game promotions on ntheumber of registration and soccer ads were more effective (P=0.04). Advertisements during soccer games had significant effect and encouragement for people on OD registration (p=0.02) but there is no significant effect from documentary programs (p=0.13). Furthermore, advertisements during soccer games are more effective when combined subtitle/host together compared to subtitle only (P=0.01). Documentaries with subtitle were more effective than without subtitles.(P =0.03).

Conclusion: Media has an improving effect on encouraging people for OD registration. But attention to the type of media used and/ or the contents of programs is important.
**P11.39**

**Knowledge and Attitudes Among Health Care Workers in the Sri Jayawardenapura General Hospital ICU Regarding Organ Donation: Do They Know Enough? A Pilot Study Developed Under the ISN-TTS STC**

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**Introduction:** Organ donation from brain-dead donors is a procedure that enables to increase life expectancy of end stage organ failure patients. As frontline workers, ICU doctors and nurses play a pivotal role in donor detection and maintenance. This study is aimed at investigating the knowledge and attitudes of ICU staff to identify the barriers for organ donation. The project was developed in the framework of the ISN-TTS (International Society of Nephrology – The Transplantation Society) Sister Transplant Center level C program, in close collaboration with the University of Barcelona and the Donation and Transplantation Institute (DTI Foundation).

**Methods:** In this cross sectional descriptive-analytical study, doctors and nurses working in ICU were included. Data collection was done by a self-administered questionnaire in July 2021. Twenty questions were based on the knowledge (K) regarding: identifying a potential donor (K1), process of brain death determination (K2), structure of deceased donation (K3), ICU care of brain-dead donor (K4) and five questions based on attitudes (A) towards donation.

**Results:** There were 44 responses, 38 from nurses and 6 from physicians. The mean knowledge regarding K1 to K4 questions was 58.9%, 57.9%, 24%, 72% respectively. The attitude (A) for donation was 68.4 %. The significant findings were that 47% believed that brain death testing was not a diagnosis of death, 81% were unaware of limb movements even after confirmed brain death and 56% were unaware of the requirement of two sets of tests for brain death diagnosis.

**Conclusion:** The study showed modest knowledge and favorable attitude toward organ donation. However, they had relatively poor understanding regarding brain death in certain concepts. Therefore, it is suggested to hold training courses to improve understanding of ICU staff of this new concept of organ donation. When passing on to level B of the ISN-TTS STC program, such trainings will be considered, and its impact will be measured.

**P11.40**

**Interstitial Glucose Metabolism Monitoring Is Additional Tool For Objective Assessment of a Donor Liver, Prediction And Immediate Diagnosis of Early Graft Dysfunction**

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**Introduction:** Current clinical practice of assessing the quality and suitability of a donor liver for transplantation does not allow to exclude cases of graft primary non-function and, at the same time, leads to an unreasonable refusal to transplant a significant number of functionally suitable organs. In this regard, an urgent task is to search for new methods for additional objective assessment and monitoring of the state of the donor organ during the peri-transplant period. The aim of the study is to determine the clinical utility of monitoring interstitial concentrations of glucose and its metabolites to assess the viability and functional state of a donor liver before and after transplantation.

**Method:** Retrospective, observational, single-center clinical study included 32 cases of liver transplantation. Along with standard methods for assessing the initial graft function, interstitial (inside the liver) concentrations of glucose and its metabolites were monitored during the first week after transplant. In 18 cases, the parameters of interstitial glucose metabolism were also studied during static cold storage (SCS).

**Results:** In cases of early allograft dysfunction (EAD), compared with normal initial graft function (IGF), statistically significantly higher interstitial lactate concentrations were observed as early as 3 hours after reperfusion: 12.3 [10.1; 15.6] mmol/l versus 7.2 [3.9;9.9] mmol/L (p=0.003). A value above 8.8 mmol/l may be considered as a criteria for the immediate EAD diagnosis (sensitivity - 89%, specificity - 65%) - Figure 1. Dynamics of interstitial concentrations of glucose and its metabolites during SCS are shown at Figure 2. Only interstitial lactate concentration at the end of SCS and the area under the curve "lactate concentration - duration of SCS" were associated with the initial graft function (Figure 3). Values greater than 15.4 mmol/l and 76.1 mmol/1h, respectively, with a sensitivity of 100% for both parameters and specificity of 77% and 85%, can be used to assess the risk of primary EAD.

**Conclusions:** Monitoring of interstitial concentrations of glucose and its metabolites, primarily lactate, is an objective additional method for the donor liver viability assessment both during SCS and in the early postoperative period.

*The study was supported by Russian Science Foundation grant (Project No. 19-75-10040).*

![Graphs showing the comparison of glucose and lactate concentrations during and after transplantation.](attachment:image.png)
Abstracts

**P11.41**

**Investigation of Optimal Temperature for Machine Perfusion of Liver Transplantation in Donors After Cardiac Death**


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**Introduction:** The usefulness of hypothermic machine perfusion and normothermic machine perfusion as preservation methods prior to liver transplantation has been reported, but is controversial. We have reported the usefulness of subnormothermic ex vivo liver perfusion (SELP) at temperatures around 20°C to 25°C, and recently we have examined the optimal conditions for perfusion time in subnormothermic oxygenated machine perfusion, but the comparison between subnormothermic machine perfusion and perfusion at other temperatures has not been examined. We evaluated organ status during machine perfusion in pigs, and investigated the optimal temperature.

**Method:** Ten F1 pigs (body weight: 27-32 kg) were induced to cardiac arrest by bilateral thoracotomy, and their livers were removed after 20 minutes of warm ischemia. The removed livers were kept cold for 2 hours and then perfused. Perfusion was performed for 120 minutes with oxygenated Krebs-Henseleit buffer using a machine (CMP-XD7W, developed by Asahikawa Medical University and Chuo Seiko Co.), which is capable of monitoring portal and arterial pressure. The group was divided into two groups according to perfusion temperature: subnormothermic perfusion group (n=5) and hypothermic perfusion group (n=5). Bile production, liver enzymes, and inflammatory cytokines were measured and the sinusoidal space, using tissue specimens taken from liver grafts, was measured at 30, 60, 90, and 120 minutes after the start of perfusion.

**Results:** LDH was significantly lower in the hypothermic perfusion group than in the subnormothermic perfusion group at all times. AST, ALT and IL-1β were not significantly different. The hepatic sinusoidal space was significantly greater in the hypothermic perfusion group at 30 minutes. Bile production was significantly lower in the hypothermic perfusion group at all time points.

**Conclusion:** Although the superiority of subnormothermic perfusion over hypothermic perfusion could not be demonstrated in this investigation, the causal relationship between organ status during perfusion and reperfusion injury is still being elucidated and requires further investigation.
P12.01

Effective Treatment of Diabetes, Improved Quality of Life And Accelerated Cognitive Development After Pancreas Transplantation in a Child With Type 1 Diabetes and Allergy To Manufactured Insulin Preparations

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Introduction: Pancreas transplantation in children is uncommon. Limited case series describe simultaneous kidney and pancreas transplants (SPK) in teenagers with type 1 diabetes and diabetic nephropathy. In the absence of indications for kidney transplantation pancreas alone transplantation (PTA) can be considered in a selected group of patients. The youngest documented recipient of PTA was 11 years old, but the graft lasted only for 6 months. Here we present the youngest PTA recipient with one-year graft survival.

Methods: A 13 years old diabetic girl with hypoglycemia unawareness and documented treatment-refractory allergy to available insulin preparations underwent a solitary pancreas transplant. Prior to the pancreas transplantation, she was receiving short-acting insulin with an increasing need for antihistamines and steroids which was negatively impacting her cognitive and social development. Her diabetes was poorly controlled and her quality of life was progressively worsening.

Results: Having the transplant she recovered well from surgery and achieved euglycemia without the need for exogenous insulin. She had two biopsy-proven episodes of acute cellular rejection successfully treated. Her cognitive development accelerated and her quality of life improved which positively her family's overall wellbeing.

Conclusions: This is the youngest, reported in the literature, pancreas transplant recipient with over one-year graft survival. Pancreas transplant alone in a teenager without indications for kidney transplantation could be considered as a last resort treatment of diabetes. The need for lifelong immunosuppression may be a reasonable trade-off in the rare scenario of failed insulin therapy and pancreas transplant is a feasible treatment modality in patients with refractory insulin allergy with no available alternatives.

P12.02

Bionic Pancetes – 3D Bioprinting of a Bionic Organ With A Vascular System – Results of Transplantation in Large Animals

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Introduction: There is lack organs for transplantation. The transplantation of the pancreas is recommended in diabetes with complications. The combination of cell biology and 3D-bioprinting can create organs with vasculature which should be functional. There are some issues to be solved: leakage, thrombosis, enhancement against high pressure, connecting organ to the recipient. The purpose of this study was to 3D-bioprint bionic pancreas which maintain a stable flow in large animals.

Material and methods: 3 pancreas geometries were calculated and bio-printed. The mechanical properties were tested in a bioreactor-20 tests. After bioprinting, the external vessels were attached: decellularized vessels(DV) and vascular prostheses(VP). Studies in animals were carried out on 5 pigs.

Results: Bionic pancreas with internal vessels of 1 mm was bio-printed. Bionic pancreas were stable up to 200 mmHg of pressure in bioreactor. In animals there was a flow throughout the organ after release of vascular clamp. In animals there was a flow throughout the organ after release of vascular clamp. In two cases(DV)-sudden stop of flow within one hour from transplantation with cloths in DV was observed. In next three cases VP were used. In third case stable flow through the organ was observed for 24 hours. Then a thrombotic clot was observed within an organ. Cloths were in the intersection between printing lines of the internal vessels which were printed transversely to the flow. The g-code and model were changed. Then stable flow was observed with ultrasound and radiographs examination during observed period in following cases.

Conclusion: 3D-bioprinted organ can be successfully fixed to the recipient and maintain flow through the organ.
P12.03
Report of the First 70 Pancreas Transplant in A Latin-American Center
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Introduction: In patients with diabetes mellitus (DBM) and end-stage renal disease (ESRD), kidney-pancreas transplantation has become an effective treatment option that reduces patient’s morbidity and increases survival compared with long-term dialysis treatment. Our aim is to show the experience in pancreas transplantation at a single center.

Methods: Patients who received pancreas transplant (PT) from April 2008 to December 2021 were incorporated for analysis. Variables analyzed included: age, sex, comorbidities, type of diabetes, types of pancreas transplants, time in waiting list, preservation solution, time of cold and warm ischemia (CI and WI), hospital and ICU length stay, complications and overall patient’s and graft’s survival. All analyses were performed using IBM SPSS v25.0.

Results: A total of 70 PT were performed at our center: 67 (95%) simultaneous pancreas-kidney (SPK), 2 (3%) pancreas transplant alone (PTA) and 1 pancreas after kidney (PAK). Thirty-six were female (51%) with a mean age of 41 ± 9 years. Fifty-three patients (76%) had type 1 DBM and the mean BMI was 24 ± 3. The estimated time in waiting list was of 8 month (range 1-69); in 50 patients (71%) the preservation solution used was Wisconsin. All PT are performed with enteric drainage. The CI and WI time were of: 389 ±173 min and 37±16 min for kidney, 487±104 min and 45±23 min for pancreas. The median ICU stay was of 7 days (range 2-67) and the total hospital stay of 18 days (range 6-121). Seventy-six kidney complications were reported in 46 patients (66%), 41 (54%) were due to urinary tract infection (UTI). Eight patients (11%) lost their kidney graft, being the most common reason cortico-resistant rejection (6, 75%). On the other hand, 64 pancreas complications were reported in 36 patients (51%), 20 of which were pancreatic fistula (31%) and 17 venous thrombosis. Fourteen patients (20%) suffered graft lost due to rejection (4, 29%) and duodenal perforation (4, 29%), 2 because of venous thrombosis (15 grafts were saved), 2 necrotizing pancreatitis 1 due to pancreatic fistula and 1 due to an hypovolemic shock. The overall pancreatic and kidney graft and patient’s survival are shown in Table 1.

Discussion: Despite a careful selection of donors and recipients, an elevated number of pancreas and kidney complications occurred. Nevertheless, under a comprehensive team approach, most result minor, and acceptable graft and overall survival can be achieved.

Patient’s at risk

<table>
<thead>
<tr>
<th>Years</th>
<th>1</th>
<th>3</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney Graft</td>
<td>90%</td>
<td>79%</td>
<td>74%</td>
<td>69%</td>
</tr>
<tr>
<td>Pancreatic Graft</td>
<td>84%</td>
<td>74%</td>
<td>72%</td>
<td>60%</td>
</tr>
<tr>
<td>Patient</td>
<td>91%</td>
<td>83%</td>
<td>81%</td>
<td>70%</td>
</tr>
</tbody>
</table>

Fig. 1. Kidney, pancreas and patient survival.

P12.04
Switch From Calcineurin Inhibitor to Belatacept in Kidney-Pancreas Transplant Recipients: Single-Center Retrospective Study From Argentina
Maira M Escobar¹, Sebastian S Rodriguez¹, Sebastián S Jaurretche J¹, Vanina V Barranco B¹, Elisa E Cerri C¹, Martin M Rodenas R¹, Ivan I Bertolin B¹, Ricardo R Pereyra P¹, Alfredo A Buschemi B¹, Jose Luis J Sgrosso S¹.
¹Renal, pancreas and heart transplant, Sanatorio Parque de Rosario, Rosario, Argentina.

Introduction: High levels of calcineurin inhibitors (CNI) have been identified as risk factors for decline in kidney function and progression to end-stage renal disease. Belatacept-treated kidney transplant recipients were less likely to have chronic kidney scarring and also had better graft function. In pancreatic transplantation, the evidence for immunosuppression regimens including Belatacept is scarce. The purpose of this study is to report the results of renal and pancreatic grafts evolution in 4 kidney-pancreatic transplant recipients who switched from CNI to Belatacept.

Method: Kidney-pancreas transplant recipient who switched from CNI to Belatacept due to renal fibrosis in graft biopsy were included. Due to the small sample size, Fisher’s Test was used to evaluate the statistical significance of the results.

Results: Four males were studied (mean age 38.25±8.64 ys). All patients received thymoglobulin induction therapy and initially maintained on steroids, tacrolimus and mycophenolate. Renal biopsy was indicated due to increased serum creatinine in 100% of population included; 1 patient also presented increased serum amylase and hyperglycemia. Three patients (75%) presented only renal fibrosis at time of the switch and the remaining patient (25%) also presented acute pancreatic rejection 1A concomitant with renal graft fibrosis. During the follow-up period after the switch (3.6±1.47 ys); 3 patients who presented isolated renal graft fibrosis maintained stable serum creatinine and adequate pancreatic graft function (p<0.05), while the patient with acute concomitant pancreatic graft rejection presented stable serum creatinine during the follow-up period but pancreatic graft loss function 28 months after the switch (p<0.05).

Conclusion: In our experience, switch from CNI to Belatacept in renal-pancreatic transplant recipients when they present renal fibrosis without pancreatic graft pathology is adequate to prevent worsening renal and pancreatic graft function. Belatacept was not an adequate maintenance immunosuppressive therapy to preserve pancreatic graft function when acute pancreatic graft rejection was present at the time of switching from CNI to Belatacept.
**P12.05**

**Bionic Pancreas - The First Results of Functionality of 3D-Bioprinted Bionic Tissue Model Transplantation With Pancreatic Islets**

Marta Klak1,2, Michal Wszola1,2,3, Andrzej Berman1,2,3, Anna Filip1, Anna Kosowska4, Joanna Olkowska-Truchanowicz4, Grzegorz Tymicki1, Michal Rachalewski1, Tomasz Bryniarski1, Marta Kolodziejska1, Tomasz Dobrzanowski5, Dominika Ujazdowska1, Jaroslaw Wejman3, Izabela Uchynowska-Tyszkievicz4, Artur Kamiński6.

1Foundation of Research and Science Development, Warsaw, Poland; 2Polibionica Ltd., Warsaw, Poland; 3Medispace Medical Centre, Warsaw, Poland; 4Medical University of Warsaw, Warsaw, Poland; 5Center for Pathomorphological Diagnostics Ltd, Warsaw, Poland.

**Introduction:** Tissue engineering is currently on an advanced stage of development which gives a possibility for novel strategy of personal treatment of type 1 diabetes.

**Aim:** In the following study, a bioink based on ECM derived from decellularization of porcine pancreas was applied for 3D bioprinting.

**Materials and Methods:** The SCID (n=60) and BALB (n=20) mice were used as a model for in vivo study. Porcine islets mixed with bioink were printed on extrusion printer and transplanted on studied animals. Effectiveness of transplanted petals with regard of their insulin secretion was evaluated based on glucose and c-peptide concentration in blood samples of studied animals. Thus, animals were divided into three groups: mice with transplanted islet-laden petals, mice with transplanted islets into kidney capsule and untreated mice. Examination of studied parameters took place at four time points during the experiment, at the beginning and on day 7th, 14th and 28th day of experiment.

**Results:** Group with transplanted petals from day 7th expressed lower mean fasting glucose concentration while compared with untreated group (129 mg/dl, 119 mg/dl, 118 mg/dl vs. 140 mg/dl, 139 mg/dl, 140 mg/dl respectively in fasting glucose concentration).

**Conclusion:** Bionic flake transplantation lowered glucose levels significantly.

**P12.06**

**Effect of Supplementing Taurine to the Developed Lowtemperature Islet Preservation Solution**

Jae-Kyung Park1, Kyungmin Kwak1, Joohyun Shim1, Nayoung Ko1, Hyoing-joon Kim1, Yongin Lee1, Jun-Hyeong Kim1, Eui-Hyun Kim1, Pulip Kang1, Jonathan RT Lakey2, Hyunil Kim1, Kimyung Choi1, 1Optipharm, Cheongju-si, Korea; 2University of California Irvine, Irvine, CA, United States.

**Introduction:** Pancreatic islet transplantation has recently emerged as one of the most promising therapeutic approaches for improving glycemic control in type 1 diabetes patients. However, one of the problems with islet transplantation is that it is impossible to culture the isolated islet for extended periods to while recipients are selected, tested and prepared for surgery. To address this problem, we developed the islet preservation solution, and to improve the function of the preservation solution, we added taurine and conducted a preservation experiment. Taurine is antioxidant activity and it is not a classical free radical scavenger. Therefore, its mechanism remains unclear but it controls osmotic pressure. Our hypothesis is that taurine supplementation can improve islet recovery and enhance islet function after low temperature preservation.

**Methods:** CMRL 1066 medium (Corning) was used as a control group, and a comparison group was prepared some compounds Opti(Optipharm preservation solution) (with taurine) and OPTI-T solution (without taurine). To confirm the preservation effect of these solutions, we isolated islet from adult Yucatan pig’s pancreas using standard enzymatic digestion (Nordmark) followed by Ficoll purification, these islets were preserved in a humidified tissue culture incubator with preservation solutions and preserved in 4°C for up to 4 weeks. We compared islet survival in groups of islets. To islet viability and islet functionality, we utilized Glucose Stimulated Insulin Secretion (GSIS) for measuring insulin release, calculated stimulation index (SI) and ACh/Pi viability staining for during the preservation period.

**Results:** Highest islet recovery was preserved in the group of pig islets cultured with Taurine as compared to the group of islets hypothetically preserved in standard tissue culture media over the 4 week preservation period (p<0.001 using ANOVA). The porcine islet viability/cell number ratio in the OPTI solution maintained a high survival rate for up to 2 weeks (94%). In contrast, porcine islet in OPTI-T solution and CMRL 1066 supplemented media significantly reduced viability after 1 weeks. OPTI solution (with taurine) was significantly higher than OPTI-T solution (without taurine) and CMRL 1066 during 4 weeks after preservation. Glucose stimulation insulin secretion test was performed for functional analysis. As a result, a level of porcine insulin was higher during 2 weeks in the OPTI solution than OPTI-T solution and CMRL 1066. But after 3 weeks preservation, insulin level in high glucose, significantly decreased. Therefore, the viability and functionality of islets were improved by adding taurine to the developed preservation solution.

**Conclusion:** Taurine supplementation has been shown to highest islet recovery, viability and insulin secretion level for 2 weeks. Based on this data, we have performed 2 weeks cold storage of isolated islets for current clinical islet transplantation.

Ministry of trade industry and energy, KEIT 20011276, NTIS 1415172664.
The Role of Pancreatic Exocrine Secretion in Weight Gain Following Pancreas Transplantation

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1Department of Surgery, Rush University Medical Center, Chicago, IL, United States.

Introduction: Weight gain after pancreas transplant is a growing concern. Weight gain can lead to post-transplant comorbidities such as diabetes type 2. A few small studies have investigated weight gain after pancreas transplantation, but none have considered the role of the exocrine pancreas. At the time of pancreas transplant, some patients maintain normal exocrine function from their native pancreases. Therefore, we hypothesized that the presence of two exocrine pancreases (native and graft) may contribute to post-transplant weight gain via supranormal levels of pancreatic exocrine secretions within the GI tract, which may contribute to increased nutrient absorption.

Methods: We performed a single-center descriptive study including patients that received pancreas transplant between June 2013 through January 2021. The operative technique was the same in all patients, with systemic vascular drainage from graft portal vein to recipient inferior vena cava, and enteric drainage of the pancreas via an anastomosis between graft duodenum and recipient proximal jejunum. Stool samples were collected from all patients at a single time-point in the post-transplant period. Stool was used to measure fecal elastase-1 (FE-1) in order to quantify the exocrine function of native and/or graft pancreas. Levels of FE-1 were correlated with levels of post-transplant weight gain.

Results: 42 patients were included in the study (Figure 1). The median FE-1 was 432 ug/g. For those with excessive weight gain (defined by >7% body weight), median was 409 ug/g. For those without excessive weight gain, FE-1 was 405 ug/g. There was no correlation between FE-1 and weight gain post-transplant. There was an inverse correlation between FE-1 and time from transplant (p=0.02), which can be seen in Figure 2. Post-transplant weight trends were similar to prior studies, where patients lost up to 8% of body weight at 1-month post-transplant and returned to baseline weight by 6 months. The largest increase in weight occurred post-transplant between years one and two.

Conclusion: Exocrine secretions appear to decrease over time following pancreas transplant. Additional prospective research, with evaluation of pre- and post-transplant FE-1 will be required to determine the influence of exocrine function on weight gain following pancreas transplantation.

Funding provided by the Department of Surgery, Rush University Medical Center.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=42)</th>
<th>FE-1 &gt;500 (n=19)</th>
<th>FE-1 &lt;499 (n=23)</th>
<th>P</th>
</tr>
</thead>
<tbody>
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<td>Gender</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30 (71)</td>
<td>13 (68)</td>
<td>17 (74)</td>
<td>0.70</td>
</tr>
<tr>
<td>Race</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>17 (41)</td>
<td>9 (47)</td>
<td>8 (34)</td>
<td></td>
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<tr>
<td>White</td>
<td>14 (33)</td>
<td>6 (32)</td>
<td>8 (35)</td>
<td>0.80</td>
</tr>
<tr>
<td>Other</td>
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<td>4 (21)</td>
<td>7 (30)</td>
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</tr>
<tr>
<td>Ethnicity</td>
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<td></td>
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</tr>
<tr>
<td>Non-Hispanic</td>
<td>31 (74)</td>
<td>13 (68)</td>
<td>18 (78)</td>
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</tr>
<tr>
<td>Age at Tx (y)</td>
<td>48 ± 10</td>
<td>49 ± 11</td>
<td>47 ± 10</td>
<td>0.43</td>
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<tr>
<td>Type of Tx</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPK</td>
<td>39 (93)</td>
<td>19 (100)</td>
<td>20 (87)</td>
<td>0.24</td>
</tr>
<tr>
<td>FAK</td>
<td>3 (7)</td>
<td>0 (0)</td>
<td>3 (13)</td>
<td></td>
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<tr>
<td>BMI at Tx (kg/m²)</td>
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</tr>
<tr>
<td>18.5-24.9</td>
<td>18 (43)</td>
<td>7 (37)</td>
<td>11 (48)</td>
<td>0.70</td>
</tr>
<tr>
<td>25.0-29.9</td>
<td>15 (36)</td>
<td>7 (37)</td>
<td>8 (35)</td>
<td></td>
</tr>
<tr>
<td>≥30.0-34.9</td>
<td>9 (21)</td>
<td>5 (26)</td>
<td>4 (17)</td>
<td></td>
</tr>
<tr>
<td>Duration of DM (y)</td>
<td>23 (16,26)</td>
<td>20 (16,28)</td>
<td>23 (19,26)</td>
<td>0.44</td>
</tr>
<tr>
<td>Pre-Tx C-Peptide (ng/mL)</td>
<td>1.81 (0.14,4)</td>
<td>3.1 (0.1,6.2)</td>
<td>0.68 (0.1,3.1)</td>
<td>0.06</td>
</tr>
<tr>
<td>Insulin Use Pre-Tx (unit/kg/day)</td>
<td>0.27 (0.16-0.5)</td>
<td>0.27 (0.05-0.57)</td>
<td>0.27 (0.05-0.7)</td>
<td>0.26</td>
</tr>
<tr>
<td>Fecal Elastase (ug Elast/g)</td>
<td>432 (326,2170)</td>
<td>2,170 (1,700,2,870)</td>
<td>333 (246,386)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figure 3. Fecal Elastase Trend Post-Transplant
Immunomodulatory Microporous Annealed Particle (MAP) Gel Protects Delivery of Islets to Promote Islet Transplantation Outcomes

Mingyang Ma1, Preeti Chhabra2, Colleen Roosa2, Donald Griffin3, Kenneth Brayman1.
1Surgery, University of Virginia, Charlottesville, VA, United States; 2Biomedical Engineering, University of Virginia, Charlottesville, VA, United States

Introduction: To investigate if coating dissociated or whole islets with microporous annealed particle (MAP) gel could support cell function and viability and improve islet transplantation outcomes.

Methods: a) C57BL/6 mouse islets were mixed with MAP gel and cultured in 24 well plates at 37°C. The viability of islets was scored after Propidium Iodide-Fluorescein Diacetate (PI/FDA) staining and Glucose stimulated insulin secretion (GSIS) assay performed on Day 1, 3, 5, and 7 post-culture. The experiment was done thrice. b) Single cells from C57BL/6 mouse dissociated islets were mixed with MAP gel, and cultured in 24 well plates at 37°C. Viability of cells was scored after PI/FDA staining and GSIS assay performed 1, 24, 48, and 72 hours post-culture. c) 100 C57BL/6 mouse islets were dissociated into single cells by Trypsin, mixed with MAP gel, and transplanted into syngeneic diabetic recipients under the kidney capsule. Blood glucose (BG) was measured daily.

Results: Mouse islets protected with MAP gel displayed similar GSIS and viability scores when compared to uncoated islets. Both groups retained above 95% viability, with the stimulation index (SI) of MAP gel-protected islets 3.2 and that of uncoated islets is 2.4. Viability of dissociated islets protected with MAP gel was 84% with a SI=8.5 at 72 hours post culture. In contrast, uncoated dissociated islets were nearly dead with only 35% viability and an SI=0.38 at 72 hours post culturing. In MAP scaffold, dissociated islet cell viability was density dependent – cell viability in the 50 and 12.5 dissociated islet conditions was on average >75%, while dissociated cells from 2.5 islets demonstrated 56% viability after 72 hours. In in vivo studies, no significant difference was observed in the ability to return Streptozotocin-induced diabetic mice to normoglycemia when either MAP gel coated or uncoated whole islets (75-100 islets) were transplanted under the mouse kidney capsule. C57BL/6 mouse islets (100 islets) that were dissociated to single cells and co-transplanted with MAP gel under the kidney capsule, permanently returned transplanted mice to normoglycemia, with glucose levels below 200mg/dL within 18 days post-transplantation (n=6). In contrast, uncoated dissociated islets failed to restore normoglycemia in transplanted mice. Treatment efficacy continued 40 days post-transplantation (time mice were monitored). The average blood glucose measured at Day 30 was 163 ± 38.2 mg/dL. Recipient mice transplanted with cells from dissociated islets without MAP gel remained hyperglycemic (n=6/group).

Conclusion: The MAP scaffold protects delivery of dissociated islet cells, and helps promote islet transplantation outcomes. Moreover, MAP scaffold provides a possible platform for delivering stem cell-derived insulin-secreting cells.

LaunchPad Ignite. NIH grant: NIBIB R21 Trailblazer [1R21EB028971-01A1].
**P12.13**

**Simultaneous Kidney and Pancreas Transplantation in Patients With Type 1 Diabetes Mellitus, Almenara Hospital Lima-Peru, 2009-2021**

Sherley Diestra

Summary: In patients with type 1 diabetes mellitus and end-stage renal failure, kidney and pancreas transplantation is the best therapeutic option.

Target: To present the clinical results in patients with type 1 diabetes mellitus and end-stage renal failure who underwent simultaneous kidney and pancreas transplantation.

Materials and methods: Since 2009, 10 kidney and pancreas transplants have been performed at the Almenara hospital, including 10 patients who underwent simultaneous kidney and pancreas transplantation. Non-parametric statistical analysis was performed and survival was estimated using the Kaplan-Meier method.

Results: Between 2009 and 2021, 10 simultaneous kidney and pancreas transplants were performed. The male gender 60%, with an age – at the time of transplantation – of 31 years, and a time elapsed from the start of dialysis support to transplantation of 61 months 70% of the population had dialysis support by hemodialysis 20% peritoneal dialysis and 10% pre-dialysis, Average age of cadaveric donor 25 years, glycemic control was achieved support by hemodialysis 20% peritoneal dialysis and 10% pre-dialysis, Average age of cadaveric donor 25 years, glycemic control was achieved support by hemodialysis 20% peritoneal dialysis and 10% pre-dialysis, Average age of cadaveric donor 25 years, glycemic control was achieved support by hemodialysis 20% peritoneal dialysis and 10% pre-dialysis, Survival of renal graft 100% per year, and that of the pancreatic graft, 90% per year, values comparable to the best expected results.

Conclusion: Simultaneous kidney and pancreas transplantation is the best surgical option for controlling complications secondary to type 1 diabetes mellitus and end-stage renal failure. The small number of the sample reflects the lack of donors, a situation that worsened with the COVID pandemic.

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**P12.14**

**Liver Surface Can Be a Promising Transplant Site For Pancreatic Islets Using a Gelatin Hydrogel Nonwoven Fabric**

Yukiko Endo, Akiko Inagaki, Takehiro Imura, Hiroaki Mitsugashira, Ryusuke Saito, Takumi Katano, Shigehito Miyagi, Takashi Kamei, Michiaki Unno, Yasuhiko Tabata, Masafumi Goto

1Department of Surgery, Tohoku University Graduate School of Medicine, Sendai, Japan; 2Division of Transplantation and Regenerative Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan; 3Laboratory of Biomaterials, Department of Regeneration Science and Engineering, Institute for Frontier Life and Medical Sciences, Kyoto University, Kyoto, Japan.

Introduction: Islet transplantation (Tx) is a promising treatment for type 1 diabetic patients. While intraportal injection is the current gold-standard method for clinical islet Tx, the renal subcapsular space is considered a preferable transplant site for experimental Tx, mostly due to the avoidance of the instant blood-mediated inflammatory reaction. As an invasive approach to the renal subcapsular space is impractical for severe diabetic patients who usually have diabetic nephropathy, a similar approach using transplant sites other than the kidney is needed. We previously reported that islet transplantation with syngeneic keratinocyte sheets onto the liver surface (LS) achieved glycemic control in diabetic rats. However, lot-to-lot variations in keratinocyte sheets and strong adhesion between the diaphragm and liver remain issues to be resolved. We therefore investigated the utility of a gelatin hydrogel nonwoven fabric (GHNF) as an effective alternative to keratinocyte sheets when islet grafts are transplanted onto the LS.

Method: Male Lewis rats were used as both donors and recipients. As experimental groups, 10 or 20 islet equivalents (IEQs)/g of recipient body weight were seeded onto the GHNF and then, placed onto the LS, and covered with an adhesion barrier (Seprafilm®; LS with GHNF 10 group [n=21] and LS with GHNF 20 group [n=6]). As control groups, intraportal injection of islets (5 IEQs/g; Ipo group, n=8), placement of adhesion barrier on the LS (AB group, n=11), and islet alone Tx onto the LS (10 IEQs/g; LS alone group, n=4) were also performed. The graft function was evaluated by the non-fasting blood glucose levels, body weight, and intravenous glucose tolerance test. Serological and immunohistochemical analyses of transplanted islets are currently being performed.

Results: No diabetic recipients were cured in the AB or LS alone groups (Fig 1). In contrast, in the Ipo and LS with GHNF 20 groups, blood glucose levels decreased promptly after Tx, and the cure rate of diabetic recipients was comparable between the groups (82.5% vs. 66.7%) (Fig 1). Notably, unlike keratinocyte sheets, adhesion between the diaphragm and liver appeared to be minimal in the LS with GHNF 20 group, suggesting that additional Tx may be feasible. However, when the dose of islets was reduced, the cure rate of LS with GHNF 10 was proportionately decreased (23.5%). The glucose tolerance was significantly better in the Ipo, LS with GHNF 20, and LS with GHNF 10 groups than in the AB group (area under the curve: 30,268±5,183, 33,578±2,783, 34,974±10,545 vs. 56,483±5,263 min·mg/dL, respectively; p<0.01) (Fig 2).

Conclusions: Given these findings, a GHNF may be a stable and effective alternative to keratinocyte sheets when islets are transplanted onto the LS. Based on the present proof of concept for liver surface Tx, this procedure in combination with an angiogenesis approach may be an attractive strategy going forward.
Dapagliflozin for the Treatment of Post-transplant Diabetes Mellitus After Pancreas Transplantation: A Case Report With A 14-Month Follow-up

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1Department of Diagnostic and Therapeutic Services, IRCCS-ISMETT (Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione), UPMC Italy, Palermo, Italy; 2Department for the Treatment and Study of Abdominal Diseases and Abdominal Transplantation, IRCCS-ISMETT (Istituto Mediterraneo per i Trapianti e Terapie ad alta specializzazione), UPMC Italy, Palermo, Italy

Introduction: Post-transplant diabetes mellitus (PTDM) is a common metabolic alteration after transplant. Almost all immunosuppressive (IS) drugs, reduce insulin sensitivity and express cytotoxicity against β-cell. The cause of hyperglycemia in pancreas transplant (PTX) can also be linked to rejection and type 1 diabetes (T1D) recurrence. However, mild hyperglycemia with preserved c-peptide and clear signs of insulin resistance (IR) should be treated using type 2 diabetes therapeutic recommendations, thus taking into account the extra-glycemic effects of the new antidiabetic drugs. In recent years, great attention has been paid to sodium-glucose cotransporter-2 inhibitors (SGLT-2i) for their cardio and renoprotective action.

Case presentation: We report the case of a male patient who underwent PTX alone in 2007, initially on IS with tacrolimus, mycophenolate mofetil (MM) and prednisone. PTX was complicated by several episodes of acute rejection and the development of lobar pneumonia. For this reason, steroid was discontinued and MM reduced. The patient is in regular pneumological follow-up and stable. Despite radiological and histological signs of rejection, the patient remained in good glycemic control until 2016 when for the first time altered home blood glucose (BG) and glycated hemoglobin (HbA1c: 6.6%) were found. On this occasion, considering the presence of a robust c-peptide, treatment with metformin was started with beneficial effect. In February 2020, HbA1c was 6.1% with a high glycemic variability and trend for hypoglycemic events secondary to therapy with repaglinide, added by other clinician 4 months before. Fasting BG was 109 mg/dl, c-peptide 1.74 ng/ml (stable for at least 5 years). Mild diabetic nephropathy was found (eGFR: 69 ml/min; albuminuria: 94 mg/L). Considering these data and the patient’s particular condition, repaglinide was discontinued and dapagliflozin 10 mg/day was associated with metformin. On March 2021 patient showed HbA1c 6.8% with normal home BG values and an improved renal function with normalization of albuminuria. No adverse events were reported.

Conclusion: Limited data in the literature describe pathophysiological mechanism and frequency of PTDM after PTX. History of T1D influences the choice of insulin as first therapeutic approach in high BG after PTX. The combination of IR and β-cell dysfunction caused by IS, T1D recurrence, and rejection contributes to the worsening of BG control. Sometimes one component prevails over the other, as in the case of our patient, who achieved BG compensation with oral agents only. The use of repaglinide as well as any other secretagogue drug is not recommended due to the rapid β-cell exhaustion after PTX. Use of SGLT-2i has allowed to maintain good glycemic control without hypoglycemia, taking advantage of renal protection and reduced CV risk. Great caution is required in this population, also considering the higher risk of adverse events as ketoacidosis and genitourinary infections.
Availability of Using Amnion for Islet Transplantation
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Amnion, a component of the placental membrane which is adjacent to the fetus, is focused on as a promising material for regenerative medicine and transplantation. Amnion includes extracellular matrix, which can be a scaffold for transplanted cells and tissues. Furthermore, amnion contains mesenchymal stem cells. They have multipotencies and play an important role in releasing various growth factors, which promote cellular growth, immune tolerance or angiogenesis. Therefore, it is considered that amnion can be an ideal scaffold for engraftment of transplanted islets. In this study, we attempt to elucidate the usefulness of amnion using animal islet transplantation model. Eight to twelve-week-old C57BL/6J pregnant female mice were used as donors of amnion and C57BL/6J male mice as donors of islets and diabetic recipients. Approximately 1.5 cm-sized amnions were used for this study. We tried to assess the effectiveness of amnion by two transplant models. The one was subcutaneous transplant model. Amnion was previously implanted into the axilla of diabetic mouse at 14 days before islet transplantation. 1 cm-sized polyethylene terephthalate tube was inserted into the inner cavity of the amnion as a spacer for transplanted islets. Five hundred islet equivalents (IEQs) were implanted into the inner cavity of amnion after removal of the spacer (amnion-assisted subcutaneous islet transplantation). The other was fat-covered transplant model. Islet (150 IEQs) were infused into inner cavity of amnion and cultured. Then, this amnion containing islets was positioned onto epididymal white adipose tissue of diabetic mice and covered by the tissue (fat-covered amnion/islet transplantation). As a result, two out of four mice received amnion-assisted subcutaneous islet transplantation and one out of four mice received fat-covered amnion/islet transplantation achieved normoglycemia. Regarding later, re-elevation of blood glucose level after graftectomy was confirmed in all four mice received fat-covered amnion/islet transplantation (459.0 ± 87.4 mg/dL vs. 711.0 ± 77.2 mg/dL, p = 0.11). Histologic assessment of recovered fat-covered amnion with islets at postoperative day 56 revealed that engrafted islets with hypervascularization were seen in epididymal white adipose tissue (Figure 1). On the other hand, there was no superiority to islet transplant model without usage of amnion in both subcutaneous and fat-covered transplant models in blood glucose level. Our study showed the possibility of amnion as a scaffold for transplanted islets, however, islet transplantation using amnion needs further improvement.

Mr. Ryo Kawakami and Mr. Yuriko Hamaguchi for histological examinations.

Figure 1. Engrafted islets in epididymal white adipose tissue in fat-covered amnion/islet transplantation at postoperative day 56. Hypervascularization was seen in and around the islets (triangles).

Simultaneous Pancreas-Kidney Transplantation in One Russian Transplant Center
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Introduction: Simultaneous pancreas-kidney transplantation (SPKT) is the best medical option to achieve stable euglycemia and insulin independence in patients with type 1 diabetes mellitus and end-stage renal disease. The outcomes of SPKT in one transplant center with the largest number of pancreas transplantations in Russia are presented.

Methods: The retrospective analysis of 79 SPKT performed at our transplant center from January 2008 to December 2021 was made. Besides, the impact of significant factors that affect the outcomes of SPKT was done. Intra-abdominal pancreas transplantation with duodenojejunoanastomosis was performed in 18 recipients (22.8%). Retropertitoneal pancreas transplantation was performed in 61 patients (77.2%), exocrine drainage was made via duodenoduodenocolonanostomosis in 50 patients (63.9%) and via duodenojejunoanastomosis in 11 patients (13.9%). In 69 patients (87.3%) vascular reconstruction with a Y-shaped graft was used, in 9 cases (11.4%) the pancreas graft with isolated splenic artery blood supply was used and the pancreas graft with triple blood supply (gastroduodenal, superior mesenteric and splenic arteries) was used in 1 recipient (1.3%).

Results: Rates of immunological and surgical complications were 25.3% and 43.4%, respectively. The rate of non-vascular complications was significantly higher than the rate of vascular complications (77.5% vs. 22.5%; p<0.001). 1-, 5- and 10-year uncensored and death-censored survival rates were 83.4%, 79.8%, 72.6% and 88.2%, 86.1%, 83.7% for kidney graft and 75.7%, 70.8%, 61.7% and 82.9%, 79.2%, 71.0% for pancreas graft. 1-, 5- and 10-year uncensored survival rates were 84.6%, 82.9% and 78.0%, respectively. The factors that significantly affected the pancreas graft survival were duration of renal replacement therapy (p=0.001), Clavien IIb surgical complications (p=0.046), reoperations (p=0.001) and kidney graft failure (p=0.001). The factors that significantly affected the patient graft survival were duration of renal replacement therapy (p=0.007), diabetes mellitus duration (p=0.006), Clavien IIb (p=0.016) and IVa (p=0.03) surgical complications, reoperations (p<0.001), kidney and pancreas graft failure (p<0.001).

Conclusion: The results of SPKTx at the N.V. Sklifosovsky Research Institute for Emergency Medicine are comparable to those in most transplant centers.
P13.01

Pediatric Liver Transplantation for Inborn Errors of Metabolism at the Hospital Juan P Garrahan, Argentina

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Introduction: Liver transplantation (LT) has become an alternative treatment for Inborn Errors of Metabolism (IEM). This approach can significantly improve quality of life of patients who suffer from severe disease manifestations and/or life-threatening metabolic decompensations despite medical management. The aim of this article was to report a single-center experience of pediatric liver transplantation for IEM.

Methods: 922 LT were performed from March 1993 to December 2021 at Garrahan Hospital in Buenos Aires. Medical records of 45 patients who suffered IEM younger than 18 years were analyzed. The variables measured were: patient demographics, indications, cirrhosis or non cirrhosis, graft type, survival, postoperative complications, growth and schooling.

Results: IEM represented 5% of the LT in 28 years. 45 LT were performed (25 females, 20 males) at a median age of 69 months (range 1-217 months). The median follow up time was 4.4 years (range 0.01-23 yr). LT indications were: cirrhosis complications (14), quality of life (23) and acute liver failure (8). Twenty-five were cirrhotic and 20 non cirrhotic in the explants. The cumulative 1, 5 and 10-year graft survival rates were 84%, 84% and 77% respectively. 23 LT were performed in IEM that affect intermediate metabolism (glycogen storage disease 8 MSUD1, argininosuccinic aciduria 3, OTC deficiency 4, citrullinemia I 2, methylmalonic aciduria 2, tyrosinemia I 4) at a median age of 91 months (range 18-210 months). The median follow up time was 2.4 years (range 0.01-23 yr). LT indication were: cirrhosis complications in 4, quality of life in 17 and 2 acute liver failure. 8 IEM were cirrhotic in the explants. 2 combined liver-kidney transplantation was performed. Biliary and vascular complications were 33% and 22% respectively. Six had a liver tumor: 3 adenomas and 3 hepatocellular carcinoma. The cumulative 1, 5 and 10 years graft survival rates were 96%, 87% and 87% respectively. If we take into account transplant periods before and after the implementation of PELD/MELD system to categorize patients by severity, we can distinguish two groups: LT before 2005 and those after. If we compare graft survival at 1, 5 and 10 years in LT globally in the pre-PELD/MELD era, this was 66, 94%, 58.87% and 52.69, respectively (N=372), after 2005 the graft survival was 81.37%, 5 years 72.10%, 66.6% (N=550). Survival before 2005 in IEM was 58%, 58%, and 33%, respectively, while after 2005 it was 93%, 93%, and 93%.

Conclusion: Liver transplantation improves the survival and quality of life in IEM. Short- and long-term survival in LT improved considerably with the implementation of the PELD/MELD System and this was more evident in the IEM group, although the follow-up intervals were shorter. The improvement in surgical techniques, immunosuppression regimens and supportive treatment may explain these differences. In the IEM group, experience in other centers and early indications for LT may explain the increased survival.

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P13.02

Significant Fall in Living Donation Rates of Pediatric Kidney Transplants in Puerto Rico

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Introduction: Living donation (LD) offers superior outcomes compared to deceased donor (DD) transplantation for patients with ESRD. In the US, an increment in LD rate was observed until 2001 and 2004, when LD rates began to decrease in ped and adult renal transplants (KTx), respectively. Knowledge about LD trends among children who have received KTx in PR is limited. We describe LD trends among pediatric KTx performed in PR from 1977-2013.

Methods: Retrospective chart review of all children (0-18yrs) receiving KTx in PR from 1977-2013. Median (range) frequencies (percentages) were calculated.

Results: From 1977-2013, 146 children, female: 39%, Hispanic: 100%, age: 14yrs (2-18yrs) were transplanted. 60% received LD and 40%DD. 75%LD were parents, 13%LD siblings, and 1%LD unrelated. 16%DD were from the US. Total number of transplants remained stable from 1980-2000 (1977-79: 5 KTx, 1980’s: 40 KTx, 1990’s: 40 KTx, 2000’s: 45 KTx) (2010-13: 16 KTx). LD rate decreased over time (77-79: 100%, 80’s: 85%, 90’s: 75%, 00’s: 31%, 10-13: 12%); 6%pts received 2nd KTx at 21yrs or younger, with 67% and 33% LD on 1st and 2nd KTx, respectively. Of these pts, female: 44%, age at first KTx: 12yrs (5,18yrs), and age at 2nd KTx: 17yrs (13-21yrs).

Conclusions: Living donation in pediatric renal transplants has substantially declined in PR over the last 4 decades. Possible explanations include single parenting, medical unsuitability, shifting practice patterns (i.e. establishment of solid organ procurement organizations), and marketing strategies, among others. Additional studies are needed to better understand the causes of such decline and to develop strategies to increase LD among our children with ESRD.

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Multidisciplinary Approach to Hepatoblastoma in Pediatric Liver Transplantation

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Introduction: Hepatoblastoma (HBL) is the most common type of liver malignancy in children, representing 80% of all liver tumors and 1-2% of pediatric tumors. The standard of care is multimodal therapy with resection of the tumors when feasible. However, recent research has shown to significantly reduce tumor size, in many of these cases the tumor is unresectable due to its extensive involvement, which leads to liver transplantation (LT). A quality assessment and improvement project and protocol was developed to emphasize the role of multidisciplinary approach and the treatment pathways for hepatoblastoma offered and the importance of team work.

Methods: Retrospective study of 24 children with diagnosis of HBL. Study period was November 1998 to March 2022. We analyzed the treatment pathways offered to these patients to assess the outcomes of multidisciplinary approach for the treatment of HBL. We evaluated demographics the PRETEXT score, therapeutic approach, patient and graft survival. Cases are discussed in a tumor board and liver selection meetings with active participation of oncology, hepatology, surgery, radiology and the multidisciplinary transplant and living liver donor (LLD) team.

Results: 24 children with diagnosis of HBL, were enrolled in a multidisciplinary approach. 54% percent were female, the median age at time of resection/transplantation was 31 months (range: 8 - 127 months) Most of them were classified as PRETEXT IV (58%), followed by PRETEXT III and II (33% and 8.3% respectively). Resection was performed in 12 patients and eventually 6 (50%) required transplantation, of these 4 were salvage LT for recurrence of disease and 2 were transplanted for complications after aggressive resection. Seven patients received transarterial chemoembolization (TACE), 4 children were downstaged and resected and 2 went to LT. Over 80% of the patients resected and/or had TACE completed standard transplant work up and were listed. Half of these had a living liver donor approved and in the last 5 years LLD available on the day of resection in case we could not obtain an R0 resection. Eighteen LT were performed in 16 patients, of the 2 patients were retransplanted (reLT), 1 was and early reLT for HAT and 1 reLT (>5 years) for chronic rejection. 1 patient is currently waiting as a Status 1b (U.S.). Median waitlist time for transplant patients was 69 days with no waitlist mortality at this point. 44% of the LT were technical variants and 25% LDLT. 80% percent of the patients are still alive and 68.5% are free of recurrence. LT survival is 75% with a mean follow-up time of 5 years. Sixty-six percent of patients who underwent salvage are alive.

Conclusions: For children with HBL it is imperative to have a constant quality assessment, multidisciplinary protocol and continuous improvement projects to ensure review and decision making with combined medical (oncology/hepatology) surgical and radiologic expertise to ensure good long term outcomes.

Association Between Vitamin D Deficiency and Anemia in Pediatric Renal Transplant Recipients

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Introduction: The relationship between vitamin D deficiency and anemia has been evaluated in patients with CKD. However, there is no study examining this relationship in renal transplantation patients. In this study, we examined the relationship between Vitamin D levels and anemia in pediatric renal transplant patients.

Materials and Methods: Records of pediatric renal transplant recipients (aged 0-18 years), who were followed up for at least one year after renal transplantation, were examined retrospectively. Transplant age, donor type, immunosuppressive treatments, infection, rejection, graft loss status and complete blood count, serum iron (Fe), serum iron-binding capacity, ferritin, urea, creatinine, calcium, phosphorus, alkaline phosphatase, parathyroid hormone (PTH) values, and eGFR values were recorded. Anemia was defined as hemoglobin level below 11 g/dl; vitamin D deficiency defined as 25 (OH)-D levels <20ng/ml; group 1, 20-30 ng/ml; group 2, >30ng/ml; group 3. Results: Seventy-five patients were included in to study. The mean age of patients was 11.8±4.9 years (34 girls and 41 boys). There were 41 patients (54.7%) in group 1, 24 patients (32%) in group 2, and 10 patients (13%) in group 3. The groups were similar in terms of gender, transplantation age, donor type, immunosuppressive therapy, and follow-up times. Mean hematocrit and ferritin levels were found to be significantly lower in group 1 when compared with the other groups (p<0.05). However, there was no significant difference between the groups in terms Hgb, serum Fe, transferrin saturation and serum Ca, P, ALP, and PTH values (p>0.05). Serum Fe levels were low in patients with vitamin D deficiency, but no statistically significant difference was found. The groups were similar in terms of infection, rejection, graft loss, and 3rd-year eGFR (p>0.05).

Anemia was present in 20(26.6%) patients and 94% of these had Vitamin D deficiency or insufficiency. In 7(12.7%) patients without anemia Vitamin D levels were within normal limits, while only 1(5.6%) of patients with anemia had normal Vitamin D levels. Vitamin D levels were found to be lower in patients with anemia. PTH and eGFR values were similar in with and without anemia group.

Conclusion: Vitamin D deficiency is a treatable risk factor for graft loss and mortality in patients with persistent anemia after renal transplantation. Further studies are needed on the relationship between Vitamin D level and anemia in renal transplant patients.
Probable Posttransplant Lymphoproliferative Disorder After Pediatric Living Donor Liver Transplantation: Is a Biopsy Still Needed?


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Background: Posttransplant lymphoproliferative disorder is a complication of solid organ transplantation and is associated with Epstein-Barr virus. Recently, Epstein-Barr virus-related posttransplant lymphoproliferative disorder was defined as probable posttransplant lymphoproliferative disorder or proven posttransplant lymphoproliferative disorder. Probable posttransplant lymphoproliferative disorder involves significant lymphadenopathy, hepatosplenomegaly, or other end-organ manifestations, without a histological diagnosis, together with significant Epstein-Barr virus DNAemia. Proven posttransplant lymphoproliferative disorder is the detection of Epstein-Barr virus-encoded proteins in tissue specimens, together with symptoms and/or signs originating from the affected organ. Probable posttransplant lymphoproliferative disorder after pediatric liver transplantation has not been well documented. Therefore, we aimed to describe the cases of five pediatric patients with probable posttransplant lymphoproliferative disorder after liver transplantation who were successfully treated with preemptive immunosuppression reduction with or without rituximab.

Case series: All five patients (age range, 1-4 years; 2 girls and 3 boys) had Epstein-Barr virus DNAemia. Three patients developed probable posttransplant lymphoproliferative disorder within 12 months of transplantation. Three patients had significantly high Epstein-Barr viral loads, but the other two patients with lymphadenopathy and end-organ manifestations had relatively low Epstein-Barr viral loads. Early-onset pediatric posttransplant lymphoproliferative disorder with significant Epstein-Barr virus DNAemia is almost universally Epstein-Barr virus-related. Biopsy was not performed due to the relative inaccessibility of the lesions and young age of the patients.

Conclusions: If the patient’s symptoms are too mild, excisional biopsy is too difficult to perform, or the patient is too sick to undergo invasive procedures, initiating preemptive treatment without a histological diagnosis could be the treatment option.

Valve Bladder Diversion, Making Possible a Kidney Transplant

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Introduction: The late diagnosis in a patient with posterior urethral valve (PUV) and end-stage kidney disease is a challenging scenario which may need renal replacement therapy and reconstruction of the urinary tract. Reducing recurrent urinary tract infections (UTI) is the main urologic objective in these patients in order to offer them a kidney transplantation (KT). Many factors must be considered to define the best moment to perform the reconstruction, that could be done prior, during or after kidney transplantation.

Patient and Method: This is a 5-year-old boy who was admitted for febrile urinary tract infection. During the admission end-stage kidney disease and PUV were diagnosed. The first step was to perform a cystoscopy and valvular ablation. Videourodynamics studies after surgery showed a bladder’s capacity of 50 ml, low compliance, incomplete emptying associated with high grade bilateral vesicoureteral reflux. Hemodialysis began as renal replacement therapy, antibiotic prophylaxis and anticholinergics were indicated. Four months later, an open vesicostomy was performed due to persistent febrile urinary tract infections. Eleven months after diagnosis, the patient was transplanted using a graft from a deceased donor. At the same time of transplant surgery, the right kidney and ureter were resected through a right hockey stick incision. Two months after transplantation another endoscopic residual valve ablation was done. After seventeen months from kidney transplant, the left kidney and ureter were resected by laparoscopy. Urodynamic studies continued showing high voiding detrusor pressure. While patient kept his bladder diverted, incontinence was managed with five diapers a day and maintained scholar and physical activities. At two years of follow-up, a third valvular endoscopic revision and ablation was performed associated with circumcision and replacing the open vesicostomy with a suprapubic tube. Intermittent opening was indicated and after three months, the tube was removed. Six months after the last surgery, bladder’s capacity improved from 100 ml to 250 ml, bladder emptying has no residual volume and no incontinence. Kidney ultrasonography did not present hydronephrosis and cystography showed no VUR. Twenty nine months after KT the patient remained urinary tract infections free, creatinine level was 0.68 mg/dL and clearance 102 ml/min/1.73 m2.

Conclusion: Open vesicostomy is a simple and safe procedure to manage UTI and allows kidney transplant in PUV valve bladders. Urological surveillance after transplant involves clinical assessment, urodynamic studies, endoscopic and reconstructive surgeries. Bladder cycling after transplant improves storage and augmentation procedures may not be needed.
P13.07

Detecting Subclinical Rejection Using dd-cfDNA in Pediatric Kidney Transplant

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Introduction: Detection of subclinical kidney transplant (KTx) rejection by surveillance biopsies and early management improves graft survival. However, these are cumbersome and invasive. Donor derived cell free DNA (dd-cfDNA) has emerged as a tool to predict KTx rejection in adult patients when >1% is present. Limited data is available in pediatrics. We aimed to determine whether surveillance with dd-cfDNA detects subclinical KTx rejection in children using a threshold >1%.

Methods: Retrospective chart review of all patients (n=30) followed at a single pediatric KTx program from 1/2021-12/2021. Patients with multiorgan transplant (n=2) and without dd-cfDNA (n=1) were excluded. dd-cfDNA was performed as surveillance, starting on 12/2020 (every 3-6 months). dd-cfDNA, demographics, eGFR, BK status, donor specific antibodies (DSA) and biopsy (Bx) findings (Banff 2019 criteria) were collected. Descriptive statistics and diagnostic test validity assessments were performed. Rejection outcome (for diagnostic validity testing) was defined as any of these: borderline T-cell mediated rejection (bTCMR), TCMR, antibody mediated rejection (ABMR), or mixed.

Results: During study period, 27 patients had dd-cfDNA performed. ESKD cause: 65% CAKUT, 31% GN; sex: 27% female; age at KTx: 12yrs; baseline eGFR: 87 ml/min/1.73m2 (IQR 78-96). Post KTx time at dd-cfDNA evaluations: 30% (n=8) < 1yr, 33% (n=9) 1-3yrs, 37% (n=10) > 3yrs. 11 patients had dd-cfDNA >1%; two of them were not biopsied (1 had BK viremia, dd-cfDNA decreased < 1% after lowering immunosuppression (IST); 1 had DSA and abnormal coagulations, dd-cfDNA decreased < 1% after increasing maintenance IST). 44% of patients (12/27) had a biopsy: 9 with dd-cfDNA >1% (median 1.8% [IQR 1.6-3.2%]); Bx findings: 3 TCMR, 4 bTCMR, 2 mixed rejection) and 3 with dd-cfDNA < 1%, performed due to another indication (AKI=2 and BK viremia=1; median 0.78% [IQR 0.7-0.8%]); Bx findings: 1 bTCMR, 1 TCMR and 1 normal. dd-cfDNA >1% had a 100% specificity and 81.8% sensitivity (AUC: 0.909) to diagnose rejection. In patients with dd-cfDNA < 1% and no Bx, median dd-cfDNA was 0.23% [IQR 0.16-0.42%].

Conclusions: Subclinical rejection was detected using dd-cfDNA >1% in this cohort with high specificity/sensitivity, supporting its potential use as a graft rejection surveillance tool. Two patients had dd-cfDNA < 1% and rejection suggesting that lower cut-offs may be needed to enhance detection. Given the small sample size and low ABMR prevalence in this cohort, we were unable to assess whether dd-cfDNA discriminates between rejection types. Validation of dd-cfDNA is needed in larger scale pediatric studies.

P13.08

Pediatric Kidney Transplantation in the Middle-East: Challenges and Solutions

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Pediatric kidney transplantation (PKT) is the best option for treating children with end-stage renal disease (ESRD). The major challenge in the Middle East (ME) countries is to provide optimal treatment to children with ESRD. Poor economics, paucity of renal replacement therapy (RRT) and transplantation facilities in the government sector and high costs in private sector render majority of children disfranchised from RRT and transplantation. Transplantation in the ME is shaped by the prevailing religious socioeconomic and health indicators. Living organ donation is the most widely practiced type of donation. However, some countries like Iran, Turkey, Kuwait, and Saudi Arabia already have their well-established deceased donation programs. Epidemiological information from the ME on the pediatric ESRD and PKT is very scant. Overall kidney transplantation rates are low in developing countries mainly due to economic and paucity of facilities. In children, rates are largely unknown and where reported are low, <0.1 per million child population (pmcp) in Pakistan and 4–5 pmcp in Kuwait. Most reports are single center experiences except few multicenter reports. The kidney graft survival in some ME centers who published their data was 88-92% at one year, 67-89% at five year, and 50-83% at 10 years post-transplant. Most of these figures are quite comparable to western data. In developed countries PKT has become a routinely successful procedure where 1- and 5-year graft survival rates are 93% and 77% from deceased donors and 95% and 85% from living donors. Low health spending, poorly developed infrastructures, delayed referral of children with chronic kidney disease, comorbidities, lacking technical expertise, inadequate pediatric dialysis programs, extended dialysis time, organ shortage, commercial transplantation, and post-transplant infections are the main pre and post-transplant challenges. The community-government partnership model has shown that pediatric RRT and transplantation can be successfully established in a developing country including many of ME countries. Society can be motivated to accept transplantation as the therapy of choice for ESRD provided the outcomes are good and it is available “free of cost” to all who need it.

In this report we present an overview of RRT in ME countries. It highlights the challenges encountered and their solutions for establishing a successful and viable pediatric transplant program in low resource. Conclusion: Although PKT is active in many parts of the ME, it is still inactive in others and mostly relying on living donors. The lacking deceased programs in most ME countries is a main issue to be addressed to adequately responding to the increasing demand for organs.
P13.09

Biliary Atresia: Intention-To-Treat Analysis in a Pediatric Liver Transplant Center

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Background: In patients with Biliary Atresia (BA), the efforts at avoiding premature liver transplantation (LT) target early identification and diagnosis, timing of Kasai-portoenterostomy (KPE) before 45 days of age, and centralization of surgery at experienced centers. However, a large percentage of infants still require LT in the first 2 years of life, and many referrals to liver transplant centers are still late.

Aim: The aim of this study was to analyze the outcomes of all patients with BA, with no previous treatment, referred to a single team, on an intent-to-treat basis.

Methods: Retrospective study in patients with no previous treatment referred to our center from Jan/2001 to Jan/2021. All the patient’s care, which included diagnosis of BA, portalenterostomy (PE), clinical follow-up, transplantation, and post-transplant follow-up was provided by the same pediatric hepatology and transplant team throughout the years. All patients included in this study had BA. They were evaluated according to their age (days) at first assessment, clinical presentation (jaundice, coluria, acolic stools), physical examination (size of the liver and spleen, presence of ascites), laboratory values (liver function tests, infectious workup, serum protein electrophoresis), image studies (total abdominal ultrasound and hepatobiliary scintigraphy - DISIDA Scan), liver biopsy, and intraoperative cholangiography when necessary. The patients were divided in three groups according to the initial assessment: LT only, Kasai portoenterostomy (KPE) only, and KPE + LT group.

Results: Thirty-nine patients with biliary atresia were followed from an early age. Seven patients did not undergo Kasai-PE, and received liver grafts at various time points (LT-only Group). Thirty-two children underwent KPE. Nine of them composed the Kasai only Group: 8 patients survived with their native liver at a median time of 5 years (range 2 to 11y), but one patient in this group died during the follow-up. Twenty-three patients were transplanted after the PE (Kasai + LT Group). Median follow-up in this group was 11 years (range 2 to 20). The overall patient survival of the entire cohort was 94.8%, and the survival with native liver was 28.1%. Interestingly, 10 patients in this series (25.6%) were babies conceived through in vitro fertilization (IVF), distributed proportionally in the observed groups.

Conclusion: This abstract shows that when all the treatment options are at hand and timely offered to patients with BA, the expected long-term results are excellent (85% patient survival). A interesting finding in this study, which has not been reported elsewhere, was the 25% association of BA and IVF.

P13.10

Secondary Ureteral Re-Implantation for Persistent Urinary Leakage Following Renal Transplantation in a Nigerian Pediatric Patient: A Case Report

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Introduction: Renal transplantation remains the gold standard renal replacement therapy for End stage renal disease worldwide and urinary leakage is an early urologic complication that may arise following renal transplantation. The site of uretero-neocystostomy is the commonest anatomical location of the leakage. Surgical intervention by renal allograft exploration and secondary uretero-neocystostomy is usually reserved for circumstances when all conservative approaches have failed. Proper diagnosis of urine leak and timely intervention will help in mitigating the attendant morbidity as well as risk of graft loss.

Case Report: A 15-year old male with ESRD secondary to chronic glomerulonephritis who had a living related renal transplantation developed significant peri-allograft urine collection and leakage from the previous drain site 5 weeks after kidney transplant. He had experienced a seemingly smooth post-operative period with timely removal of his wound drain and Doppler ultrasound scan confirming a satisfactory renal allograft function. His renal function had normalised three days following transplant with serum urea and creatinine values of 5.4mmol/L and 96umol/L respectively. Few days following the removal of the double J stent, he had a progressively increasing peri-allograft collection, worsening pain, and swelling over the transplanted area with oliguria and drainage from the surgical scar. Initial conservative treatment of the urine leak by urethral catheterization and percutaneous drainage of the collection under image guidance were unsuccessful. He has a re-exploration with secondary uretero-neocystostomy and is doing very well.

Conclusion: Urine leak remains a common urological complication in the early post-transplant period and the manifestation can be delayed up to 1 month Post –transplantation following removal of DJ stents. There may be need for open surgical intervention if conservative treatment is unsuccessful. Timely open surgical exploration of the allograft is associated with a good outcome with minimal morbidity and less risk to allograft function when non-operative management fails.
The Largest Single Center Report on Hypertyrosinemia And Liver Transplantation

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Introduction: Hereditary tyrosinemia type 1 is a rare autosomal recessive metabolic disorder with an estimated incidence of 1/100,000 to 1/120,000 worldwide. We aimed to evaluate the outcome of liver transplantation in patients with tyrosinemia.

Methods: This study was conducted in the Shiraz transplant center, affiliated to Shiraz University of Medical Sciences, in Abu Ali hospital, Shiraz, Iran. All pediatric patients who underwent liver transplantation for tyrosinemia were included in this report.

Results: Overall 107 patients entered this study. The majority of patients were male (56%) with a median age of 36 months. Median (IQR) duration of liver disease was 19 months and median hospital stay was 2 days. Approximately, 14.9% of patients had cirrhosis in their first liver biopsy. Among tyrosinemic patients, 3 had HCC in histologic examination of the explanted liver. Median Pediatric end-stage liver disease (PELD) score at transplant was 13. Most of the participants had Child-Pugh class A (63.1%) with a mean score of 6.41 ± 1.9. Mean warm ischemic time and cold ischemic time was 45 and 80 minutes, respectively. Median follow-up duration was 54 months. During the study, 29 patients died which was mostly due to sepsis (34.5%). The overall 1-, 2-, 5-, and 15-year survival rates were 85%, 77.5%, 77.6% and 77.6%, respectively. The majority of our donors were living donors (51.4%).

Conclusion: This is the largest single-center report on pediatric liver transplantation and tyrosinemia.
Pediatric Transplant and SARS COV2 in a Country With High Lethality

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Introduction: At the time of reporting, Peru has 3,522,444 cases of SARS CoV 2 infection, with a lethality of 5.98%. The official data are 1315 deaths from 0-19 years of age (10-19 years: 700; 53.99%; male). While 74% of the population is fully vaccinated, coverage in the pediatric population is still low: 5-11th: 52.17% (1 dose) and 25.17% (2 doses); 12-17th: 82.334% (1 dose) 68.79% (2 doses) 0.83% (3 doses). Among those awaiting transplantation and transplanted (regardless of age) 1725 (1 dose), 1244 (2 doses) and 227 (3 doses, 13.16%).

Methods: We describe a case series of pediatric transplanted patients (kidney and liver) between March 2020 and December 2021, the population was 114 patients, being the sample 58 patients who met the criteria for the study (pediatric age, SARS CoV2 infection).

Results: 32.76% of pediatric transplant recipients were infected with SARS CoV2. The highest number of cases was in January 2022 (31.58%: 6), 57.89% were female. The mean age for liver transplant recipients was: 10.7 years and for kidney transplant recipients: 14.5 years. 63.16% (12) had between 4 to 9 years post-transplantation and only 7.69% (1) had less than 3 months post-transplantation. Most frequent symptoms: rhinorrhea, cough and diarrhea. Complications: pneumonia. Comorbidities: Diabetes Mellitus (1), HTA (1). The 94.74% (18) were blood group O+. Regarding the HLA in renal patients: A (2.24/2.68) B (35/61/ 35.39) DR (4.8), they needed hospitalization: 2 (13.33%), 1 in mechanical ventilation (MV). In relation to immunosuppression: in 61.54% the use of antiproliferative drugs was reduced and suspended in 13.33%, while the use of corticoids was maintained. Of the vaccinated patients, 46.15% were infected. One patient obituated at the beginning of the pandemic who was the first transplanted patient in the hospital to become infected.

Conclusions: Despite the pandemic and the restrictions imposed by the government and hospital regulations and the shortage of donors in the country it was possible to perform 12 transplants (41.66% with living donor), however, they were not the most affected in this pandemic, which reinforces the importance of maintaining isolation. Mortality in pediatric transplant recipients was similar to that of the country (5.26%). Despite vaccination, there were cases of infection in vaccinated patients, which will show the authorities that pediatric transplant recipients should receive booster vaccination.

Liver Transplantation in Alagille Syndrome With NOTCH2 Genetic Variant: Case Report

Luciola Vasquez, Bertha Cardenas, Martin Padilla, Carlos Rondón.

Introduction: Alagille-Watson Syndrome, an autosomal dominant multiorgan disease, with a frequency of 1/30000; presents an alteration in the NOTCH receptor pathway, considering the transmembrane proteins: JAGGED1 (JAG1) and NOTCH2 the affected ones. The study of chromosome 20 (short arm) has been able to identify variants in this pathway, reporting mostly alterations in the JAGGED1 ligand and between 2-4% in the NOTCH2 receptor. The genetic alteration in the NOTCH2 receptor is less clear, being the major missense type, so that cardiac characteristics, vertebral alterations and facial features are expressed with less prevalence.

Method: Case Report.

Results: Female patient who presented jaundice since she was 3 months old. At 7 months she underwent a surgical biopsy, with findings: hypotrophic gallbladder, no extrahepatic biliary tract was observed. Liver biopsy: ductular proliferation in all portal spaces; cholestasis in hepatocytes, canaliculi and ducts; slightly active micronodular cirrhosis with ductopenia. Laboratory: urea creatinine dissociation, hypertriglyceridemia; with parameters in ranges of malnutrition. At 18 months of age, being considered a ductopenic syndrome, she was sent abroad to undergo liver transplantation with a living donor (Hospital Austral-Argentina). Upon return to our center and during the follow up, a genetic study was performed in which the NOTCH2 gene was reported, with the variant c.4316G>A (p.Cys1439Tyr), heterozygous, of uncertain significance; this variant presents a substitution of Cysteine for Tyrosine in codon 1439 of the NOTCH2 protein (p.Cys1439Tyr) and during the follow up, a genetic study was performed in which the NOTCH2 gene was reported, with the variant c.4316G>A (p.Cys1439Tyr) heterozygous, of uncertain significance; this variant presents a substitution of Cysteine for Tyrosine in codon 1439 of the NOTCH2 protein (p.Cys1439Tyr) (Invitae #: R02577430; Invitae Corporation, San Francisco, CA 94103).

Conclusion: With the identification of this gene the patient has a definitive diagnosis of Alagille syndrome with NOTCH2 gene involvement with an uncommon, rare variant (p.Cys1439Tyr).

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Experience in Pediatric Renal Transplantation. Guillermo Almenara Irigoyen National Hospital- Lima, Peru. 2009 - 2021

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Introduction: 91% of transplants in Peru are performed by the Social Security (EnSalud), the percentage of pediatric renal transplants ranges between 8-14.57% with respect to adults. In 2009, the Renal Transplant Service of the Organ Transplant Department of the Guillermo Almenara National Hospital began transplants in children (under 18 years of age), with 19 children benefiting in the first phase (2009-2013) and 50 children in the second phase (2014-2021). At the time of the report, 70 pediatric renal transplants were performed.

Objective: To describe the experience in pediatric renal transplantation in a Social Security Hospital.

Material and methods: Descriptive study of case series from January 2009 to December 2021.

Results: Total patients 69, Total renal transplants 70. Waiting time for cadaveric donor ranged: 7.7 (2-36months). Mean age: 11.8 (range: 5-17years). Sex: 63.16% female. 47.37% were from the province, The etiology was: Renal hypoplasia/dysplasia: 23.68%, Uropathy: 18.42%, Glomerulopathy: 28.94%, Non-affiliated: 10.42%, Others: 18.42% (Vasculitis, cryoglobulinemia, mic syndrome, Alport syndrome, Autosomal recessive polycystic disease). Renal replacement therapy: hemodialysis: 81.58%, Pre dialysis: 5.26%. Lowest recipient weight: 12kg. Living related donor was 50%. Duplo transplant (Liver-Kidney): 1.43%. Renal graft: 24.3% was right, 1.42% en bloc. 20% had 2 and 2.86%: 3 arteries. Ureteral catheter was used in 51.4%. Bladder size in 21.4%. Immediate complications: vascular thrombosis 4.28%, graft dysfunction 1.42%. During the follow-up 12% of infection by Poliomavirus was reported, Diabetes de Novo: 4.34%, Recurrence of glomerulopathy (FSGS): 2.89%. All received induction, being Polyclonal(Thymic) 32.86%; Maintenance therapy was: Tacrolimus, Mycophenolate Mofetil, Prednisone (the latter was withdrawn in some with renal malformations), Graft loss was: Vascular thrombosis: 2.89%, humoral rejection: 4.28% Chronic dysfunction: 5.71%. These losses were in the age group: 15-18 years. Overall survival: patient 98.5% and graft survival at 1, 5 and 10 years: 94.2%, 91.4% and 87.14% respectively. Patient loss was due to SARS Cov2.

Conclusion: 4.28% of graft losses occurred when transferred to adults. The low number of cadaveric donors increased with related living donor, with 4.28% of graft losses occurred when transferred to adults. The experience of the Center allowed us to perform the first double transplant in a pediatric patient in the country.
Clinical Features and Outcomes Following SARS-cov-2 Infection in Pediatric Liver Transplant Patients

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Introduction: Several studies suggest that chronic immunosuppressive treatment in pediatric liver transplant recipients may predispose to increased risk of acquiring SARS-CoV-19 infection, however, the severity of the infection and mortality rates remains unclear due to the lack of sufficient clinical data. Herein, we assessed the severity and clinical features following SARS-CoV-19 infection in our pediatric liver transplant recipient’s cohort.

Methods: We assessed total of 118 pediatric liver transplant recipients between 1-18 years of age who had been followed between 01 March 2019 to December 2021. Demographic data, clinical and laboratory features were obtained from electronic medical record as well as the state health record system. The information regarding the severity of the symptoms, duration of hospitalization, and outcomes of the infection were obtained by telephone inquiries. Patients with COVID-19 infection prior liver transplantation, unknown hospitalization status or unconfirmed SARS-CoV infection were excluded. The demographic, clinical and laboratory features of the patients were analysed descriptively.

Results: A total of 16 out of 118 (13.5%) pediatric liver transplant recipients were diagnosed with COVID-19 infection. Eleven (68.8%) patients were male with a median age of 14.8 (interquartile range, 8-16) years. The main presenting symptoms were as follows; fever in 8 (50%), cough in 6 (37.5%), sore throat in 4 (25%), runny nose in 5 (31.3%), myalgia in 3 (18.8%), and abdominal pain in 2 (12.5%) patients. None of the patients exhibited respiratory failure, arthralgia, smell and taste loss, or diarrhea. Out of 16 COVID-19 patients, 6 (37.5%) had complete blood count, biochemistry tests and coagulation profile. Four of them exhibited leukopenia and mildly elevated C-reactive protein. One patient required computed tomography of thorax due to respiratory distress which revealed the ground-glass opacity and minimal pleural effusion. Only 3 out of 16 patients required hospitalization with a mean 2.67-days length of stay. Two out of 16 patients received favipiravir and two patients required antibiotics treatment due to suspected pneumonia. No SARS-CoV-19 infection associated intensive care admission or death were observed in our study. Nine out of 16 patients with SARS-CoV-19 were unvaccinated due to following reasons: 8 patients were younger than 12 years as vaccination is not recommended in this age group by the current guidelines of the Turkish ministry of health, and 1 patient was recently tested positive for COVID-19 infection. Rest seven out of 16 patients had two doses of COVID-19 vaccination.

Conclusion: In this study, pediatric LT patients with SARS-CoV-19 infection showed a wide range of clinical presentations while the outcomes of the infection were generally mild.

Our Pediatric Liver and Kidney Transplant Activities in 2021

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Introduction: In children with end-stage renal disease, chronic liver failure or acute liver failure, liver (LT) and kidney transplant (KT) is the most effective modality leading to better clinical outcomes compared to other medical or replacement therapies. On the other hand, since solid organ transplantation in children may cause complications at a higher rate, it should only be performed in centers with experience and multidisciplinary expertise. In this study we aimed to assess our LT and KT activities in 2021.

Material and Methods: Between 3 November 1975 and 31 December 2021 we have performed 701 LT and 3290 KT. 382 of these KT and 334 of these LT were pediatric. On March 15, 1990, the first living donor pediatric liver transplant was performed by our team in Turkey, Europe and the region. Between 01 January 2021 and 31 December 2021 we performed 21 LT and 114 KT. 19 of the LT and 12 of the KT we performed in 2021 were pediatric. We recorded age, gender, body mass index (BMI), comorbidities, etiologies, laboratory values and clinical outcomes of the recipients.

Results: Between 01 January 2021 and 31 December 2021 we performed 19 pediatric LT and 12 pediatric KT. The mean age of the LT recipients was 3.4 years. Eight of these recipients were male. The most common etiology was biliary atresia (n=7). All of LT’s were living related liver transplant and all recipients were relatives with their donors. The mean length of hospital stay was 17.6 days. Except 2 patients all recipients discharged successfully. 2 LT patients died in the early postoperative period due to sepsis. The mean age of the KT recipients was 14.1 years. Four of these recipients were male. The most common etiology was vesicoureteral reflux (n=3). Except one, all of KT’s were living related kidney transplant and all recipients were relatives with their donors. The mean length of hospital stay was 4.3 days. All recipients discharged successfully.

Conclusion: Although transplant procedures for young children are more complex, they can be performed successfully in experienced transplant centers.
Decrease Incidence of Typical Hemolytic Uremic Syndrome As A Cause for Kidney Transplantation in Children at Garrahan Hospital

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Introduction: In Argentina, hemolytic uremic syndrome (HUS) is an endemic disease. It is the second most common cause of kidney transplantation (KTx) in children. Although an improvement in sanitary conditions could reduce its incidence, this does not seem to occur in recent years. For more than three decades, protective measures have been introduced to reduce kidney sequelae and delay progression to end-stage renal disease (ESRD). If this were so, it should be reflected in a reduction in the cumulative incidence of KTx due to HUS. On the other hand, there is little information on the evolution of HUS in the post-transplant period compared to other etiologies of ESRD.

Aim: 1. To determine whether cumulative incidence of KTx in children with ESRD secondary to HUS has decreased over time in a series of 1000 transplants over 33 years, and if HUS continues to be the second cause of ESRD in these patients. 2. To compare patient and graft survival at the last follow-up visit in children transplanted for HUS.

Material and Methods: A retrospective cohort study was conducted including 1000 consecutive KTx performed at Hospital Garrahan between December 14, 1988 and August 18, 2021. All the cohort was divided into quintiles (Q), in each quintile cumulative incidence of HUS was compared to ESRD related to other etiologies. It was also analyzed in the different five-year periods of the transplant program. Patient and graft survival was compared to those with other etiologies of ESRD.

Results: Analyzing the cohort of children with KTx in different quintiles, HUS continued being the second-most common cause for KTx in Q1 (1988-1995), Q2 (1996-2003), and Q3 (2004 - 2009). In Q4 (2010-2015) and Q5 (2016-2021) HUS became the third cause. Comparing the proportion of patients with HUS to those with other etiologies of ESRD in Q1, Q2 and Q3 vs Q4 and Q5 this number decreased over time: Q1: 17% (n=34/200; p < 0.001), Q2: 13.5% (n=27/200; p = 0.004), Q3: 11.5% (n=23/200; p = 0.03) and Q4 and Q5 10.5% (n=20/200) and 3% (n=6/200), respectively. Cumulative incidence of patients undergoing KTx because of HUS was 10.97%. In era 1 (KTx performed in Q1, Q2 and Q3) cumulative incidence was 14% vs 6.45% in era 2 (Q4 and Q5; p = 0.0002). Mean decrease of the risk of requiring KTx because of HUS was 54% (95% CI: 30-70%; p=0.0002) No significant differences were found in age at dialysis initiation (8.9±4 vs 8 ±5 years; p=0.79) and at KTx (11±4 vs 12±5 years; p=0.18). Patient survival was not different between groups (p=0.15). Graft survival in HUS vs CAKUT group was not different (p=0.61), but significantly better compared to those with FSGS (p<0.001).

Conclusion: In this cohort, a decrease in cumulative incidence of KTx because of typical HUS was observed. This lower incidence may be due, at least in part, to measures to prevent ESRD. Graft survival was similar in HUS and CAKUT patients, but significantly better compared to those with FSGS.
P14.01

Cryobiopsy in the Diagnosis of Lung Allograft Rejection: Brazilian Case Series


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Introduction: Bronchoscopy with transbronchial biopsy is the main tool for diagnosing lung allograft rejection and is also used in lung transplantation recipients follow-up. Recent trials have shown a higher sensitivity value in cryobiopsy than transbronchial biopsy for allograft rejection.

Method: Four cases of lung transplantation in a single center in Brazil were analyzed for allograft rejection with transbronchial cryobiopsy. The materials were examined by the same pathologist in all cases and the results were based on the 2007 International Society for Heart and Lung Transplantation (ISHLT) grading for allograft rejection.

Results: Four pulmonary transplanted patients were submitted to transbronchial biopsy, which either resulted inconclusive (Ax according with ISHLT grading for allograft rejection) or inconsistent with clinical manifestations and pulmonary function. As an outcome, those patients underwent cryobiopsy to investigate allograft dysfunction. All of them had their rejection grading modified after the procedure and therefore their treatment which consisted in pulse therapy with methylprednisolone. The characteristics of the patients are described in Table 1.

Conclusion: Cryobiopsy is an accurate procedure for diagnosing cellular allograft rejection post lung transplant and can change treatment for patients.

P14.02

Viability of Native Kidney in Cardiorenal Transplantation


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Introduction: Renal failure can be present in up to 50% of patients (P) with chronic heart failure. Combined Cardiorenal Transplant (CCRTx) is indicated in Heart Transplant candidates (HTx) with Chronic Kidney Disease (CKD). According to the latest update of the International Society for Heart & Lung Transplantation 2016 guidelines (ISHLT), the cut-off value for estimated Glomerular Filtration Rate (eGFR) is below 35 ml/min/1.73 m2 or equal. In our Institution, the cut-off value continues to be less than or equal to 40 ml/min/1.73 m2.

Objectives: To evaluate the renal function of native kidneys by radionuclide in P with CCRTx. Analyze the eGFR cut-off value to define the candidacy for CCRTx.

Materials and methods: Between February 1993 and October 2019, CCRTx patients were evaluated retrospectively. After one year from transplantation, radionuclide was performed to assess the viability of native kidneys. Patients with CKD Stage V KDIGO 2012 (Kidney Disease Improving Global Outcomes) were excluded.

Results: Out of 587 HTx patients, 27 P (4.6%) received a CRTx. According to the inclusion criteria, 11 P were analyzed. Age 62 year-old (IQR 55-63). Men 10 P (90.9%). Six P (54.5%) had ischemic cardiomyopathy. The prevalence of cardiovascular disease risk factors was: smoking 9 P (81.8%), high blood pressure 7 P (63.6%), diabetes 2 P (18.2%). Emergency transplantation 5 P (45.4%); urgency 4 P (36.4%) and elective 2 P (18.2%). All patients received induction treatment with thymoglobulin and continued during follow-up with a triple immunosuppression scheme (calcineurin inhibitors, antiproliferative, and steroids). Minimization with mammalian Target Of Rapamycin (m-TOR) was indicated in 8 P (72.7%). Analysis of radionuclide showed loss of native kidney function in 90.9% of CCRTx patients.

Conclusion: The loss of native kidney function evidenced in radionuclides confirmed the benefit of Combined Cardiac Renal Transplant for the majority of recipients selected under our protocol.
The Usefulness of Non-HLA Monitoring During Graft Rejection Surveillance in Heart Transplantation

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Introduction: The development of Donor Specific Antibodies against Human Leucocyte Antibodies (HLA-DSA) is one of the major causes of allograft dysfunction and rejection in solid organ transplants. However, many patients diagnosed with biopsy-proven Antibody-mediated rejection (AMR) do not have HLA-DSA. Many recent studies suggest that Non-HLA antibodies are involved in the immunopathogenesis of allograft rejection and poor graft survival. Anti-vimentin and myosin antibodies presence has been associated with AMR and anti-arginine, keratin, and tubulin antibodies with acute graft rejection. Therefore, performing continuous monitoring to detect the development of both anti-HLA and non-HLA DSA would be of paramount importance.

Aims: □To analyze the presence of Non-HLA DSA in a group of heart transplant (HTx) patients with a diagnosis of AMR and absence of HLA-DSA, □To compare the Non-HLA antibodies prevalence in this group with HTx patients without rejection and absence of HLA-DSA.

Methods: Post-transplant 8 serum samples from 7 HTx recipients diagnosed with AMR by endomyocardial biopsy (EMB) and HLA-DSA absence in serum samples, were selected to be tested for Non-HLA antibodies. Nine HTx patients without rejection and HLA-DSA absence were also analyzed as a control group. The presence of DSA was determined by a single antigen bead assay using the Luminex platform (IMMUCOR) and interpreted with MATCH IT! Software. Non-HLA Antibodies were tested by Lifecodes Non-HLA Antibodies Kit (IMMUCOR) using Luminex platform and analyzed by LNHLA Analysis Tool. The AMR diagnosis was determined using the International Society for Heart and Lung Transplantation (ISHLT) grading scale updated in 2013. Biopsies were performed at the same time as the serum samples.

Results: The results of the Non-HLA antibody test of the patients who presented rejection in the EMB were compared with the control group that did not have biopsy-proven rejection results, evaluating the number of non-HLA antibodies detected in the study group compared to the control group.

Conclusions: Although the number of patients analyzed in this study is reduced, we can observe that in all the patients who presented AMR without HLA-DSA, anti-Non HLA antibodies were detected, in comparison with the control group without rejection, where the majority of the patients analyzed did not present antibodies. Regarding the Non-HLA antigens described more frequently associated with HTx rejection, we have not found this association in our group of patients, which we consider is due to the small number of samples in our study group. Our goal is to continue expanding the study group to extensively analyze our HTx patient population for non-HLA antibodies in the setting of rejection to determine the feasibility of using this assay as an additional tool in HTx graft rejection surveillance.
Lung Transplant: Supply or Demand Problem? Description of Real Donor Patients in a Public Hospital of the Argentine Republic

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Introduction: Lungs are the organs with the greatest difficulty to be transplanted. The selection criteria are strict since its subsequent implementation is difficult.1-3 In Argentina, during 2021, 23 double-lung transplants and 12 single-lung transplants were performed. Up to February 16, 2022, there were 286 subjects on the lung transplant waiting list in our country, reflecting a significant difference between recipients and donors.4 The objective of this study is to describe the clinical-demographic characteristics of actual donor patients and to evaluate the relationship between potential and actual lung donors in a public hospital in the Argentine Republic.

Material and method: Descriptive design study. Data was obtained from the electronic medical record. Real donor patients from our institution were included between January 1 and December 31, 2021. An analysis of all demographic variables necessary to be able to classify as potential lung donor according to the criteria of the Spanish Transplant Society was performed, A descriptive statistical analysis was made.

Results: 42 real donor patients were included, of which 29 (69%) were effective. Table 1 shows the clinical-demographic characteristics.

Applying the eligibility criteria, 15 potential lung donors were identified, of which 9 met ideal criteria and 6 as marginal donors. Table 2 compares patients who meet the criteria as potential lung donors with those who do not. Of the patients identified as potential donors and presented as candidates for lung ablation, only 2 (13%) were accepted and implanted.

Conclusion: At the “Hospital del Bicentenario de Esteban Echeverría” during the year 2021, 13% of all lungs that met ablation criteria were accepted and implanted. This represents an extremely low percentage considering the difficulty that lungs present in being suitable to ablation. This leads us to question why the offered lungs are rejected and what measures should be taken to increase the number of ablated organs.

Agradecimiento al Dr. Adrian Tarditti por su labor en el desarrollo de nuestra institución y haciendo posible la realización de dichos trabajos de investigación.
P14.05


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Introduction: Cerebral circulatory arrest initiates a proinflammatory cascade that impairs organ function. At the respiratory level, the increase in intravascular pressure damages the alveolar cells and increases vascular permeability. Mechanical ventilation (MV) generates stress and increases the circulation of inflammatory mediators. Respiratory muscle inactivity and supine position predispose to atelectasis, alteration of ventilatory mechanics and gas exchange. The abolition of the cough reflex hinders the hygiene of the airway, generating a risk for the lungs. The inflammation, the drop in oxygenation and the hemodynamic alterations will affect the rest of the organs, reducing their quality or even making them unfeasible for transplantation. Donor ventilation seeks to preserve the lung and reduce the damage caused by MV. There is evidence that demonstrates the benefits of the prone position in patients with Acute Respiratory Distress Syndrome: improvement in gas exchange, increased functional residual capacity, optimization of perfusion, decreased pulmonary stress and mediastinal compression. Considering the difficulty in obtaining lungs for transplantation, the use of the prone position in potential donors would reverse the deleterious effects described, increasing the availability of lungs suitable for donation. The objective of this work is to report the case of a patient to whom the prone position was applied from the diagnosis of BD.

Material and method: Case report type study at the Bicentenario Esteban Echeverria Hospital during March 2022.

Case presentation: Male, 25 years old, with no relevant history, with chronic otitis (45 days). Admitted on guard for tonic-clonic seizures, without subsequent recovery. Glasgow score 3/15. Brain abscess contiguous to the inner ear and generalized edema were identified. Irreversible cessation of brain functions was diagnosed within the first 24 hours of hospitalization. He received antibiotic treatment since admission. On day 1 of MV he had PaO2/FiO2 287 and Crs 46 ml/cmH2O. The prone position was established. On day 2 of MV he had PaO2/FiO2 509 and Crs 63.7 ml/cmH2O (Figure 1). He did not require vasopressor support nor did he present organic dysfunction. After 48 hours of antibiotic treatment, the lungs were distributed.

Conclusion: The change of position from supine to prone improved both the mechanics of the respiratory system and gas exchange. The patient went from meeting marginal criteria to ideal criteria to donate lungs and was accepted for organs distribution, even lungs.

Agradecimiento al Dr. Adrian Tarditti por su labor en el desarrollo de nuestra institución y haciendo posible la realización de dichos trabajos de investigación.

P14.06

Lung Procurement: Inclusion of Modern Variables to Assess Its Quality. Descriptive Study in a Public Hospital of the Argentine Republic

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Introduction: Over time, the selection criteria for lungs suitable for procurement have been modified. Marginal criteria have even been determined in order to increase the number of potential lung donors. Despite flexibility in the selection criteria, there have been no significant differences in the long-term mortality of patients implanted. In spite of modifications, the PaO2/FIO2 index together with a chest X-ray continue to be the only tools for assessing the state of the lung. The objective of this study is to describe modern variables that might allow identifying the state of the lung in a group of potential lung donor patients in a Public Hospital of the Argentine Republic.

Materials and Methods: Descriptive design study. Data was obtained from the electronic medical record. Patients with a diagnosis of brain death who met the criteria for potential lung donors according to the criteria of the Spanish Transplant Society were included. They had been admitted in our institution between January 1 and December 31, 2021. The following variables were analysed: PaO2/FIO2 index, Respiratory System Compliance (Csr), Ventilatory Ratio (Rv) and Index y/y. A descriptive statistical analysis was carried out.

Results: 15 patients were included, of which 9 (60%) met ideal criteria and 6 (40%) marginal criteria as lung donors. Table 1 shows the clinical-demographic characteristics. Of the six who met marginal criteria, four were due to time greater than 72 hours of MV, one for PaO2/FIO2 <300 and another one for being a smoker <20 p/year. Table 2 describes the outcome variables and the ventilator setting of the included patients.

Conclusions: Results show that despite having a good PaO2/FIO2 relationship, there is great variability in the other variables. This leads to the following questions: Can the PaO2/FIO2 variable independently define the quality of a lung? Should new variables be incorporated when choosing a potential lung donor?

Agradecimiento al Dr. Adrian Tarditti por su labor en el desarrollo de nuestra institución y haciendo posible la realización de dichos trabajos de investigación.

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**Table 1. Participants’ characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Potential lung donors (n=15)</th>
<th>Ideals (n=9)</th>
<th>Marginal (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>13 (86.6%)</td>
<td>7 (77.7%)</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Age, mean (SD), years</td>
<td>34.7 (14.4)</td>
<td>32.7 (12.5)</td>
<td>37.6 (17.8)</td>
</tr>
<tr>
<td>Charlson, median (IQR), score</td>
<td>0 (0-4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Traumatic brain injury, n (%)</td>
<td>4 (26.6%)</td>
<td>3 (33.3%)</td>
<td>1 (16.6%)</td>
</tr>
<tr>
<td>Height, mean (SD), cm</td>
<td>172 (9)</td>
<td>168.66 (7.1)</td>
<td>177.5 (9.6)</td>
</tr>
<tr>
<td>Actual weight, mean (SD), Kg</td>
<td>76 (15.5)</td>
<td>70.11 (10.6)</td>
<td>82.5 (19.7)</td>
</tr>
<tr>
<td>BMI, median (IQR)</td>
<td>25.4 (22.5-27.4)</td>
<td>25.4 (24.2-26.9)</td>
<td>25.5 (22.5-29.3)</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1 (6.6%)</td>
<td>0</td>
<td>1 (16.6%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Obesity</td>
<td>1 (6.6%)</td>
<td>0</td>
<td>1 (16.6%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory</td>
<td>0</td>
<td>1 (16.6%)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Days of MVA (ventilation) median (IQR) | 3 (2-3.5) | 2 (2-3) | 5.5 (2-7.7)

References: SD (Standard Deviation), IQR (Interquartile range), BMI (Body mass index), MVA (Mechanical Ventilatory Assistance)
P14.07

Use of Grafts With Extended Ischemic Time (Above 4 Hours Or More): Analysis of the Experience of the Largest Brazilian Heart Transplant Center, From 2013 to 2022

Ronaldo Honorato Santos1, Fabio A Gaiootto1, Samuel P Steffen1, Domingos D L Filho1, Shirlyne FD Gaspar1, Fernando Bacal1, Fabio B Jatene1
1Cardiothoracic Department - Cardiovascular Surgery Division - Heart Transplant Nucleus, Heart Institute - University of São Paulo Medical School, São Paulo, Brazil.

Introduction: The use of grafts harvested over a long distance, with ischemia time above 4 hours, is a routine in our center, the Institute of the Heart of São Paulo, the largest transplant center in Brazil. The shortage of donors, the large number of recipients (90% in national priority) and the high mortality rate on the waiting list, pushes and encourages us to use these hearts.

Objective: We evaluated transplants performed from January 2013 to March 2022, with hearts harvested at long distance, using static preservation (hypothermic) and with ischemic time greater than 4 hours, some longer than 5 hours. We evaluated survival rates, the main causes of mortality and the PGD rate, in this extended ischemic time group.

Material and methods: From January 2013 to March 2022, 396 heart transplants were performed. All grafts were preserved using static hypothermic method and the solution used was Custodiol. Preservation routine was: cardiac arrest in the donor, one the new infusion in the back-table and the grafts were brought immersed in the protection solution. The "no ice touch" technique was also used for additional protection of grafts. A total of 68 transplants (17.17% of the total) used grafts with more than 4 hours of ischemia. Of the long-distance transplants, 58 (85.29%) were with grafts with ischemic time up to 5 hours and 10 (14.70%) were performed with ischemic time greater than 5 hours.

Results: Of the 68 transplants performed with hearts with ischemic time equal to or greater than 4 hours, 58 (85.29% of this group and 14.64% of the general total) were with a time between 4 and 5 hours and 10 (14.70% of the long ischemia group and 2.53% of the overall total) were with more than 5 hours. There were 16 deaths (23.52%) in this extended ischemia time group: 13 deaths (22.41%) in the group of 4 to up to 5 hours and 3 deaths (30%) in the group with ischemia greater than 5 hours. Of the 13 deaths (19.11% of the total group with extended ischemia time) 6 deaths were due to infection (46.15%), 3 deaths were due to PGD (23.07%), 2 deaths were stroke (15.38%), 1 death was of undetermined cause (in the 63 POD) 1 death was due to ABO mismatch. Of the 3 deaths in the group with ischemia time up to 5 hours, 2 deaths were due to infection (10%) and 1 death was due to PGD (10%).

Conclusions: Despite the risks and difficulties imposed by this modality (logistics mainly), the scarcity of organs, high mortality rate on the waiting list and the large number of patients prioritized in our institution, we believe that this routine contributed with a significant number of transplants (about 17.17% of all transplants). The main cause of mortality was infectious and the PGD rate was 6.77%. These results in this special group (ischemic time equal to or greater than 4 hours - or even longer) motivates us to continue this model. Access to new preservation technologies, especially the dynamics, can optimize this modality in our country even more.

### Table 2. Ventilatory setting and monitoring of oxygenation variables

<table>
<thead>
<tr>
<th>Potential lung donors (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWB, mean (SD), Kg</td>
</tr>
<tr>
<td>Tidal Volume (ml/kg of PWB), mean (SD)</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min), median (IQR)</td>
</tr>
<tr>
<td>Peak inspiratory pressure (cm of water), median (IQR)</td>
</tr>
<tr>
<td>Plateau pressure (cm of water), mean (SD)</td>
</tr>
<tr>
<td>PEEP (cm of water), mean (SD)</td>
</tr>
<tr>
<td>Driving pressure (cm of water), mean (SD)</td>
</tr>
<tr>
<td>Static Compliance (mL/cm of water), mean (SD)</td>
</tr>
<tr>
<td>Maximal inspiratory resistance (cm of water/L/sec), median (IQR)</td>
</tr>
<tr>
<td>PaO2/FiO2 ratio, mean (SD)</td>
</tr>
<tr>
<td>Mechanical Power, median (IQR)</td>
</tr>
<tr>
<td>Ventilatory Ratio, mean (SD)</td>
</tr>
</tbody>
</table>

### Ablation day

<table>
<thead>
<tr>
<th>Potential lung donors (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal Volume (ml/kg of PWB), median (IQR)</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min), mean (SD)</td>
</tr>
<tr>
<td>Peak inspiratory pressure (cm of water), mean (SD)</td>
</tr>
<tr>
<td>Plateau pressure (cm of water), mean (SD)</td>
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<tr>
<td>PEEP (cm of water), mean (SD)</td>
</tr>
<tr>
<td>Driving pressure (cm of water), mean (SD)</td>
</tr>
<tr>
<td>Static Compliance (mL/cm of water), mean (SD)</td>
</tr>
<tr>
<td>Maximal inspiratory resistance (cm of water/L/sec), mean (SD)</td>
</tr>
<tr>
<td>PaO2/FiO2 ratio, mean (SD)</td>
</tr>
<tr>
<td>aA, mean (SD)</td>
</tr>
<tr>
<td>Mechanical Power, mean (SD)</td>
</tr>
<tr>
<td>Ventilatory Ratio, mean (SD)</td>
</tr>
<tr>
<td>Static Compliance &gt; 40 mL/cm of water, n (%)</td>
</tr>
<tr>
<td>aA &gt; 0.5, n (%)</td>
</tr>
<tr>
<td>Ventilatory Ratio &lt; 1.5, n (%)</td>
</tr>
</tbody>
</table>

References. PWB (Predicted body weight); SD (Standard Deviation); MVA (Mechanical Ventilatory Assistance); PEEP (Positive end-expiratory pressure)
Outcomes of Heart Failure Patients Excluded From Heart Transplant Waiting List

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Background: Every year the number of heart transplant recipients increases but the number of patients in the heart transplant waiting list (HTx WL) does not slow down. However, there are no data on those excluded from HTx WL. The aim was to study clinical differences of chronic heart failure (CHF) patients who excluded from a HTx WL and estimate their survival.

Methods: We retrospectively analyzed HTx WL data that was collected from 2010 to 2020 and included 280 patients: 47.4±12.8 year-old, male –210 (75%). We estimated the number of excluded patients, causes of the exclusion and patients’ clinical characteristics. Data was analyzed by using the SPSS 21.0.

Results: During 10-year follow-up 53 patients (class III by NYHA, class 2 UNOS) excluded from HTx WL: 66% (n=35; 55.4±12.5 year-old; n=33 - male) – improved (group 1), 9% (n=5; 50 [37;56] year-old; male) refused after the inclusion for their personal reasons (group 2) and 25% (n=13; 58 [46;63] year-old; n=12 - male) – due to diagnosed contraindications (group 3). Most common cause of CHF was ischaemic heart disease (49%, 60% and 69%, respectively). Patients excluded from HTx WL due to their improvement in 17 [8;43] days. lVEF were 21 [17;24] %, 13 [10;17] % and 18 [16;28] %, respectively, (p1,2=0.013) and PASP - 44±20 mm Hg, 45 [43;47] mm Hg and 59 [8;43] days. LVEF were 21 [17;24] %, 13 [10;17] % and 18 [16;28] %, respectively, (p1,2=0.013) and PASP - 44±20 mm Hg, 45 [43;47] mm Hg and 59 [8;43] days. The inclusion in HTx WL, patients completed the SF-36 questionnaire and results did not show significant differences between the groups (p>0.05). One year survival after exclusion was 86% in the group 1, 20% - group 2 and 38% – group 3. Two years after the exclusion 2 patients were put back on HTx WL and then successfully underwent heart transplantation. Mortality of excluded individuals was associated with a higher level of PAWP (n=0.72, p=0.01), a low level of venous oxygen saturation of the central venous blood (n=0.80, p=0.02), heart rate (n=0.61, p=0.03) and QRS width (n=0.52, p=0.04).

Conclusions: In 10 years 19% of patients were excluded from HTx WL, most of them due to the improvement and this one had a higher survival. Most of patients excluded due to irreversible PH but those who decided to refuse had the lower LVEF. Clinical characteristics, except LVEF and right heart failure, were similar between excluded ones.

Donor-Derived Cell Free DNA Is Associated With Antibodymediated Rejection and Impaired Cardiac Hemodynamics in Patients With Heart Transplantation

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Introduction: Donor-derived cell-free DNA (ddcfDNA) has emerged as a non-invasive biomarker for the detection of acute cellular rejection (ACR) and antibody-mediated rejection (AMR) in heart transplant (HT) recipients. Nevertheless, data regarding the clinical application of this method in a real-life setting are lacking. The aim of the present study is to assess the relationship between ddcfDNA levels, ACR, AMR and cardiac hemodynamic parameters in a European real-life cohort of HT recipients.

Method: Among the patients who received a protocol or for-cause endomyocardial biopsy (EMBx) in the period 2017-2021 at our center, we selected those with available biobanked plasma as part of the CLIN-HEART registry. ddcfDNA was measured using MiSeq Illumina platform, according to the AlloSeq cfDNA protocol (CAREDx, San Francisco, CA, USA). Pulmonary arterial wedge pressure (PAWP), right atrial pressure (RAP) and cardiac index (CI) were assessed at the time of the EMBx. Significant rejection was defined as ACR grade ≥2 and AMR grade ≥1, according to International Society for Heart and Lung Transplantation classification.

Results: DdcfDNA assessment was performed in 66 recipients. Median ddcfDNA levels were significantly higher during the first month after HT (0.33% [IQR 0.19 to 0.47] in the first 30 days vs. 0.17% [IQR 0.12 to 0.23] after 30 days from HT, p=0.004). Rejection was detected in 19 (28.8%) patients, in whom median ddcfDNA levels were 0.23% (IQR 0.16 to 0.38%). Starting from 30 days after HT, ddcfDNA levels were higher in recipients with AMR (p=0.04, Figure 1) as compared to those without. However, no significant relationship was found between ACR and ddcfDNA levels (p=0.78, Figure 2). With regards to cardiac hemodynamics, HT recipients with rejection and ddcfDNA levels above the median had a higher PAWP (15 mmHg [IQR 14 to 17 mmHg] vs. 10 mmHg [IQR 8 to 13 mmHg], p=0.04) and RAP (9 mmHg [IQR 7 to 11 mmHg] vs. 4 mmHg [IQR 2 to 6 mmHg], p=0.03), but not CI (3.07 l/min/m2 [IQR 2.90 to 3.58 l/min/m2] vs. 3.28 l/min/m2 [IQR 2.62 to 4.29 l/min/m2], p=1.00), as compared with those with ddcfDNA levels below the median. Conversely, in recipients without rejection, there was no significant association between ddcfDNA and PAWP, RAP or CI.

Conclusions: In a European real-life cohort of HT recipients, ddcfDNA levels were higher during the first month after HT and decreased thereafter. Starting from 30 days after HT, AMR but not ACR was associated with higher ddcfDNA levels. Finally, high ddcfDNA levels were associated with hemodynamic derangements only in patients with rejection.
Heart Transplant Quilty Lesions Are Associated With an Immunologic Tolerant Profile

Jose Torrealba1, Luis De Las Casas1, Qi Cai1.
1Pathology, University of Texas Southwestern, Dallas, TX, United States.

Background: Quilty lesions (QL) are tertiary type lymphoid/mononuclear cell aggregates found sporadically in heart transplant biopsies with or without associated rejection. Their role is not well understood. In this study we aimed to characterize the inflammatory phenotype and immunomodulatory pathways associated with QL.

Materials and Methods: Forty two (42) endomyocardial allograft biopsies were included in this study. Biopsies were scored by the ISHLT criteria for rejection, and immunolabeled for the T-cell markers CD4 and CD8, and the immunoregulatory markers Foxp3 and TGFβ1 for quantification. A subset of 9 biopsies, 5 with QL and 4 without QL were additionally analyzed for mRNA expression. Multiplexed mRNA measurement was performed using the nCounter system (NanoString Technologies, Seattle, WA), and data were analyzed with nSolver software (NanoString Technologies, Seattle, WA).

Results: We demonstrated that the presence of Foxp3+ innate and TGF-β+ adaptive regulatory lymphocytes in Quilty lesions are associated with higher heart allograft acceptance. Effector CD4 and CD8 positive T-cells were increased in biopsies with rejection. Out of 771 gene mRNA levels measured in the NanoString Transplant Immunology Panel, 274 were upregulated in the Quilty group over the control group, with approximately one third related to adaptive immunity and 5% to innate immunity. Higher levels of mRNA expression in the Quilty group were also shown in pathways for hematopoiesis (11%), cytokine (9%), chemokine (7%), cell-extracellular matrix interaction (7%), and apoptosis & cell cycle regulation (5%). More specifically, the mRNA expression of tolerance-associated immunity markers, including FoxP3, TGF-β, and CTLA4, were higher in the Quilty group (2.82, 1.42, and 3.97 fold increase, respectively, with p < 0.05). Markers of rejection-associated immunity, including IL-2 and INF-g, although lower in the quilty group, were not statistically different.

Conclusions: Heart allografts with Quilty lesions have dominant adaptive immunity related mRNA expression with significantly higher mRNA expression of tolerant immunity markers. These data suggest that Quilty lesions, far from passive bystanders, may serve an immunomodulatory role in cardiac allografts. The presence of intra-allograft regulatory T-lymphocyte related signaling in Quilty lesions may help to reduce the risk of rejection and foster allograft acceptance.

This work was possible with the support of Drs. George and Anne Race Distinguished Professor of Pathology Endowment Fund (Dr. Jose Torrealba).
**P14.11**

**Lung Transplantation in Adult Patients With Bronchiectasis**

Esteban Wainstein², Gladys Kahl², Maria L. Orazi², Horacio M. Castro², Juan Montagne¹, Enrique Beveraggi¹, Graciela Svetliza², Juan Montagne¹, Alejandro Da Lozzo¹, Micaela Raices¹, Enrique Beveraggi¹.

¹General Surgery, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; ²Internal Medicine, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

**Introduction:** Data regarding microbiology and outcome of patients with non-cystic fibrosis bronchiectasis (NCFB) after lung transplantation (LTx), compared with cystic fibrosis (CF), are limited. Recent data suggest that outcomes are similar between both populations.

**Methods:** We performed a retrospective analysis, from January 2010 to December 2020, of all patients undergoing LTx for bronchiectasis at our center. Microbiology of sputum specimens, lung function and clinical parameters pre- LTx were assessed. In hospital mortality was compared between both groups.

**Results:** Baseline data are summarized in table 1. 19 CF and 5 NCFB were transplanted. Chronic infection with P. aeroginosa was more common among CF patients. In hospital mortality was higher in NCFB patients.

**Conclusion:** Study population was small. Unlike other reports, in hospital mortality was higher among NCFB patients, despite a lesser presence of P. aeruginosa and antibiotic resistance. Mortality was driven by infection unrelated to colonization. Data are shown as median.

**TABLE 1.**

Baseline characteristics and outcome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CF</th>
<th>NCFB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td>Sex, female</td>
<td>8 (42%)</td>
<td>3 (60%)</td>
</tr>
<tr>
<td>BMI Kg/m²</td>
<td>19.9</td>
<td>21.4</td>
</tr>
<tr>
<td>FEV1% predicted</td>
<td>23.8</td>
<td>26</td>
</tr>
<tr>
<td>Chronic infection</td>
<td>19 (100%)</td>
<td>4 (80%)</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>18 (95%)</td>
<td>3 (60%)</td>
</tr>
<tr>
<td>SAMR</td>
<td>9 (47%)</td>
<td>0</td>
</tr>
<tr>
<td>SAMS</td>
<td>7 (39%)</td>
<td>1 (20%)</td>
</tr>
<tr>
<td>B.cepacia</td>
<td>6 (32%)</td>
<td>0</td>
</tr>
<tr>
<td>Multiple drug resistance</td>
<td>11 (58%)</td>
<td>1 (20%)</td>
</tr>
</tbody>
</table>

**TABLE 2.**

Outcome

<table>
<thead>
<tr>
<th></th>
<th>CF</th>
<th>NCFB</th>
</tr>
</thead>
<tbody>
<tr>
<td>In hospital mortality</td>
<td>4 (21%)</td>
<td>3 (60%)</td>
</tr>
</tbody>
</table>
P14.14

The Experience of Physical Activities in Lung Transplant Recipients: A Qualitative Study

Puling Wang1, Hongxia Liu1, Fucong Peng1, Changyun Wei1.
1School of Nursing, Beijing University of Chinese Medicine, Beijing, People’s Republic of China.

Introduction: Lung transplantation is an important treatment for end-stage lung disease. In the post-discharge rehabilitation stage after transplantation, recipients may experience impaired maximal exercise capacity and skeletal muscle function due to the effects of prolonged bed rest and immunosuppressive drug therapy. Physical activity can effectively improve health outcomes and quality of life in lung transplant recipients. Understanding the attitudes and experiences of lung transplant patients towards physical activity can help nurses formulate targeted individualized exercise guidance programs and improve patients’ participation and compliance in physical activity. Therefore, the aim of this study is to describe the experiences of physical activity in lung transplant recipients.

Methods: A qualitative study with a phenomenology approach was undertaken with lung transplant recipients who had admitted for follow-up review. Semi-structured interviews were conducted with 14 lung transplant recipients. Interviews were conducted by face-to-face and recorded and then transcribed verbatim.

Results: Four dominant themes and 9 subthemes were identified:
1. physical activity preferences: preference for low-intensity exercise, preference for single activity pattern;
2. perceived benefits for physical activity: promoting health and recovery, gaining a positive sense of self-identity;
3. barriers to physical activity: health-related issues, psychological factor (disappointment with the effects of physical activity, fear of physical activity), external environmental factors;
4. motivating factors for physical activity: desire to restore health; family support.

Conclusion: Physical activity is an effective supplementary treatment method for lung transplant recipients. Nursing staff should mobilize multi-channel support to help patients overcome obstacles to physical activity; pay attention to patient experience and provide individualized care; promote patients to develop physical activity habits and improve long-term rehabilitation compliance.

The LT recipients who participated in this study.

P14.15

Early Preventive “Coronary Sealing” of Transmitted Coronary Artery Disease With Stent PTCA to Improve Outcomes of Heart Transplantation

Sergey V Gautier1, Alex Shevchenko1, Nadia N Koloskova1, Boris L Mironkov1, Anna J Goncharova1.
1Cardiology, Shumakov National Transplant Centre, Moscow, Russian Federation.

Introduction: The prevalence of asymptomatic coronary atherosclerosis in the population is high, and the use of donor hearts from older individuals and “suboptimal” donors increases the likelihood of coronary artery disease (CAD) transmission to the heart recipients. Percutaneous transluminal coronary angioplasty (PTCA) with subsequent stenting improves angina symptoms but has no advantages over medical therapy in the “native heart” CAD patients. We hypothesize that early preventive coronary angioplasty would improve prognosis of the insensitive denervated donor hearts patients.

Objectives: To study the impact of transmitted CAD and preventive angioplasty on the risk of death, re-transplantation, or the need for coronary revascularization in the long-term period after orthotopic heart transplantation (HT).

Methods: All recipients who received the heart transplant at the Shumakov National Transplant Centre (Moscow, Russia) between January 2013 and December 2016 and survived 30 days after the surgery were included. Initial endomyocardial biopsy and coronary angiography were performed at the first week. Patients with >50% stenosis in the large branches of the coronary arteries were randomized to receive immediate PTCA or not. All-cause death, re-transplantation due to irreversible heart graft dysfunction, and the need for PTCA were used as a primary outcome composite endpoint.

Results: A total of 431 HT were performed from 15.01.2013 to 29.12.2016; 389 (90.3%) patients have survived 30 days after HT; 10 (2.3%) patients who underwent repeated HT within 30 days were not included in the study. 389 (90.3%) patients have survived 30 days after HT; 10 (2.3%) patients who underwent repeated HT within 30 days were not included in the study. The prevalence of asymptomatic coronary atherosclerosis in the population is high, and the use of donor hearts from older individuals and “suboptimal” donors increases the likelihood of coronary artery disease (CAD) transmission to the heart recipients. Percutaneous transluminal coronary angioplasty (PTCA) with subsequent stenting improves angina symptoms but has no advantages over medical therapy in the “native heart” CAD patients. We hypothesize that early preventive coronary angioplasty would improve prognosis of the insensitive denervated donor hearts patients.

Conclusion: The study showed that the presence of the occlusive (>50%) stenotic coronary segments in the donor’s heart has significant effect on event-free survival after HT and preventive PTCA of these segments improves the risk of death and re-transplantation while increases the likelihood of repeated coronary revascularization in the future.
Acute and Chronic Allograft Rejection in the Uruguayan Lung Transplant Program in the 2003 – 2022 Period

Isabel Villanueva1, Nicolás Tommasino1, Cecilia Chao1, Ana Musetti1, Pablo Curbelo1.
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Introduction: Lung transplant (LT) is a therapeutic option able to improve the survival and life quality in patients with refractory chronic lung diseases up to maximum treatment. After the first post LT year the major cause of death is the chronic lung allograft dysfunction (CLAD). Acute rejection (AR) has an incidence of 28% in the first year post LT according to ISHLT and increases the CLAD risk. The objective of this article is to describe the events of AR and CLAD in the population of the uruguayan LT program in the January 2003 – March 2022 period.

Methods: Descriptive and retrospective study of transplanted and re-transplanted patients. 45 transplants were performed, including 3 re-transplants, 6 patients who died due to another cause in the first month after LT were excluded.

Results: The characteristics of the patients and their transplants are exposed in Table 1. More than half of LT occurred in the last 5 years. The median conditional survival of the program is 7.5 years. There were 29 cellular RA (CAR) events in a total of 19 patients (48.7% of the total); 12 patients presented 1 event, 4 patients 2 events and 3 patients 3 events. These events occurred: 10 in the first month post LT (34.5%), 5 between 1 and 3 months (17.1%), 7 between 3 months and 1 year (24.2%), 7 after the first year (24.2%). Rejection level was A1 in 55.1%, A2 in 41.4% and A4 in 3.5%. The diagnosis was made through surveillance endoscopies in 22 events (75.8%), the remaining diagnoses were made in the context of suspected rejection. 23 of the events (79.3%) were asymptomatic, while in the other ones presented as cough, expectoration, and/or dyspnea, being the infectious cause the main differential diagnosis. 17 patients (58.6%) received treatment, 10 cases due to grade of CAR ≥ A2; the remaining patients despite their lower level, presented symptoms, spirometric and/or imageology disturbance, justifying this behavior. Intravenous methylprednisolone were done in 5 patients and oral corticoids in the remaining 12 patients. It is interesting to mention that one patient (2.2%) suffered hyperacute rejection dying 48hs after LT and other one (2.2%) humoral AR. This patient received plasmapheresis and immunoglobulin, with satisfactory evolution. 13 patients (44.8%) developed CLAD (Table 2), 9 cases (69.2%) had at least one previous CAR event. 12 of the 13 cases occurred in the first 5 years. All of them had symptoms and functional impairment as presentation form. All received azithromycin and 10 of 13 montelukast. 3 patients were transplanted due to CLAD, 2 developed BOS again.

Conclusion: CAR incidence is comparable to other Latin-American centers but significantly higher than the ISHLT reported. AR is a recognized risk factor for CLAD therefore is necessary to lower the incidence. More studies are needed to know the cause of this high rejection rate reported.
P15.01
Posterior Reversible Encephalopathy Syndrome in Transplant Patients: Diagnosis and Management

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Introduction: Posterior reversible encephalopathy syndrome (PRES) is a rare neurotoxic status composed of own brain imaging patterns. Depending on the location of the lesion, is characterized by a wide scale of neurologic symptoms. Although, the main cause of PRES is not fully enlightened, it is shown that, especially in solid organ transplant patients due to calcineurin inhibitors (CNI) toxicity, severe hypertension and any kind of infections are strongly related with PRES. The current therapy accepted is only supportive care. In this study we aim to evaluate diagnosis and management of PRES in our transplant patients.

Method: From 3 November 1975 to 31 December 2021, we performed 3288 kidney transplant, 701 liver transplant and 142 heart transplants. Among these transplants 381 patient in kidney,334 patient in liver and 70 patients in heart were pediatric. 785 pediatric transplant patients were examined, and PRES was observed in 12 pediatric patients with median age 12 years (5 month - 18 year). 6 (50%) of these patients were male and median BMI is 18.5 (12.4 - 28.9). The radiology report database was analyzed for patients which PRES was cited in brain MR imaging text reports. Cases of PRES were included and searched for demographic values, laboratory values, clinical presentation, immunosuppressive they use, management we made and results.

Results: Among PRES cases, 6 (50%) patients were liver transplant, 4 (33%) were kidney transplant and 2 (17%) were heart transplant patients. %66,5 (n:8) of the patients were using Tacrolimus as immunosuppressant. Causes of PRES were toxicity of Tacrolimus in 3 (25%) patients, hypertension in 4 (33%) patients, sepsis in 2 (16%) patients, hypomagnesemia in 1 (8,5%) patient, hyponatremia in 1 (8,5%) patient and cyclosporine toxicity in 1(8,5%) patient. Symptoms of PRES were Seizure in 8 (66,5%) patients, vision change in 3 (25%) patients, status epilepticus in 1 (8,5%) patient and nausea/ vomiting in 1 (8,5%) patient. The average time between transplant and the diagnosis of PRES was 23 days (2 - 27 days). In brain MRI edema (n:5), hemorrhagic lesions (n:4), ischemia (n:1) and brain infarction (n:1) were observed. As medical treatment all patients consulted with pediatric neurology. Patients having hypertension (n:4) are treated with antihypertensives ACEI combined with calcium canal blockers. Seizure is controlled with hydantoin at early period and levetiracetam (36,9mg/kg/day) as maintenance treatment. Patients having hypertension are taken to hemodialysis. Also, patients related with tacrolimus toxicity (n:3) were switched to cyclosporine and the patient who had cyclosporine toxicity was switched to tacrolimus. End of the treatment period all patients were discharged successfully.

Conclusion: PRES is a rare diagnosis which is having an unknown etiology and due to that doesn’t have a proven management strategy. When the patient is suspected of PRES, MRI should be performed immediately, in order to avoid complications, achieve a better recovery and treat PRES successfully.

P15.03
Granulocyte Colony-Stimulating Factor With or Without Immunosuppression Reduction in Neutropenic Kidney Transplant Recipients

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Introduction: Neutropenia, defined as an absolute neutrophil count (ANC) of < 1,500/mm3, is a common complication after kidney transplantation (KT). It is associated with adverse graft and patient outcomes, yet little is known about the best management practices for neutropenia in transplant recipients. We aimed to analyze the effect of granulocyte colony-stimulating factor (G-CSF) use with and without immunosuppression reduction on graft outcomes in neutropenic KT recipients.

Methods: We conducted a retrospective cohort study of adult (age ≥18), deceased donor recipients of KT between September 1, 2011, and December 31, 2016, who developed neutropenia within the first-year post-KT. We excluded multiorgan transplant recipients, those who were undergoing re-KT, those with a history of HIV, or primary nonfunction. Clinically significant neutropenia was defined as 1) Two consecutive ANC of < 1500/ mm3; or 2) One ANC value < 1500 cells/mm3 associated with a decrease in maintenance immunosuppression within 30 days of detection of neutropenia. Severe neutropenia was defined as an ANC < 500/mm3.

Results: We identified 120 recipients with neutropenia, within the first-year post-transplant. Of these, 45.0% underwent no intervention, 17.5% had immunosuppression reduced, 18.3% were only given G-CSF, and 19.2% had both interventions. Overall, 61 patients experienced the composite outcome of de-novo DSA, biopsy-proven acute rejection, and all-cause graft failure and the cumulative incidence of this outcome did not vary by any of the four interventions (p=0.93) (Figure). When stratifying the cohort by G-CSF use alone, those who received G-CSF were more likely to have had moderate (46.7% vs. 42.7%) or severe neutropenia (51.1% vs. 12.0%, p=0.001), and were more likely to have had immunosuppression reduction (51.1% vs. 28.0%, p=0.003). However, the composite outcome was not different in the G-CSF and no G-CSF cohort (53.3% vs. 49.3%, p=0.67), and in a multivariate model, G-CSF use was not associated with this outcome (aHR=1.18, 95%CI:0.61-2.30).

Conclusion: We conclude that G-CSF use with or without immunosuppression reduction was not associated with graft outcomes; however, this observation warrants prospective evaluation.
Human Primary Renal Tubuloids as Tools for Calcineurin Inhibitor Nephrotoxicity Assessment

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Background: Although calcineurin inhibitor(CNIs) is the most widely used immunosuppressive agent in kidney transplantation, its nephrotoxicity affects the long-term survival of kidney transplant recipients. To assess the individualized nephrotoxicity of CNIs, we performed the assessment using a method of generating renal tubuloids from the renal tissue of patients.

Methods: Primary human kidney tissue derived from biopsy specimens of living donor kidneys. Mince the tissue into pieces of~1 mm3 size using scalpels and digest pieces of tissue into cell pellets using collagenase. The cell pellets were then transferred into media containing matrigel, B27 supplement, R-spondin, epidermal growth factor, fibroblast growth factor-10, N-acetylcysteine, A83-01 and Y-27632. Tubuloids were cultured for several days, re-seeded in 96-well plates, and treated with CNIs(tacrolimus) at doses of 0, 20, 40, or 60µM for 24 hours. Morphological changes, Cell viability and KIM-1 expression were evaluated.

Results: Generation of human tubuloid cultures is identified by immunohistochemical staining for markers expressed in the tubular epithelium, such as paired box 8 protein (PAX8). The 3D structure of the kidney tubuloids and cell viability decreased in dose-dependent manners after treatment with CNIs(tacrolimus). Treatment with CNIs(tacrolimus) increased KIM-1 expression in a dose-dependent manner.

Conclusions: We generated renal tubuloids from patient kidney tissue. This method can evaluate the nephrotoxicity of CNIs in renal transplant patients and provide a possible new way for the personalized medicine of immunosuppressive agent.
Distinct FOXP3 Gene Expression in the Peripheral Blood And Inside Renal Allografts Is Associated With Use of MTOR Inhibitors and Extended Criteria Kidney Donor

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Background: Trafficking of regulatory T cells (Tregs) modulate inflammatory response after kidney transplantation. There is scarce information on whether circulating and intragraft Tregs are similarly affected by immunosuppressive drugs (ISD) and by the type of deceased kidney donor.

Objectives: 1- to study the simultaneous gene and protein expression of the FOXP3 (forkhead-winged helix transcription factor) in the peripheral blood (PB) and within renal allografts; 2- to correlate FOXP3 expression with the immunosuppressive drugs (ISD) used and kidney donor type.

Methods: FOXP3 gene and protein expression were assessed by real-time PCR and immunohistochemical analysis in the peripheral blood (PB) and kidney biopsies (Bx) of patients receiving Tacrolimus (Tac; n=21) or Everolimus (Eve; n=19) at the 3rd month post-Tx. FOXP3 expression was correlated with donor type (standard – SCD or extended criteria – ECD donors), ISD, acute rejection (AR), delayed graft function (DGF), and serum creatinine (sCr) at one year.

Results: Eve-treated patients had a longer DGF duration (p=0.04) and a lower frequency of de novo post-Tx diabetes (p=0.03) compared with the Tac group. FOXP3 expression in the PB and Bx was greater in Eve than in Tac-treated patients. Immunohistochemistry did not show differences in the FOXP3 expression for both types of ISD. Recipients of SCD and ECD had similar gene and protein expression inside allografts and in the renal tissue regardless of the ISD. However, in the PB, ECD recipients treated with Eve (ECD/Eve) had higher FOXP3 expression than ECD/Tac (p=0.04) and Everolimus (Eve; n=19) at the 3rd month post-Tx. FOXP3 expression was correlated with donor type (standard – SCD or extended criteria – ECD donors), ISD, acute rejection (AR), delayed graft function (DGF), and serum creatinine (sCr).

Conclusion: FOXP3 gene and protein expression does occur differently in the blood and inside allografts from recipients of ECD kidneys treated with mTOR inhibitors. We suggest caution when interpreting studies comparing outcomes based on the measurement of the FOXP3 gene expression in different tissues and compartments and kidney donor types.
P15.07  
Risk Prediction Model for Immunosuppressive Medication Nonadherence in Kidney Transplantation Recipients  
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Objective: To identify the risk factors associated with immunosuppressive medication (IM) nonadherence in kidney transplantation recipients and to develop a simple and effective personalized risk prediction model of it.  
Methods: A total of 1011 kidney transplantation recipients in a tertiary hospital in China were recruited from March 2020 to April 2021. Least absolute shrinkage and selection operator (Lasso) regression analysis was used to screen the optimized variables. Multivariate Logistic regression analysis was applied to develop a risk prediction model for IM nonadherence in kidney transplantation recipients, and the relevant nomogram was drawn. The receiver operating characteristic curve (ROC), calibration curves, and Hosmer-Lemeshow test were used to validate and evaluate the discrimination and calibration of the model, and Bootstrap method for internal verification.  
Results: The multivariate regression analysis showed that age, perceived barriers to adherence score, marital status, family income, medical insurance, preoperative drinking history and gender were the risk factors for IM nonadherence in kidney transplantation recipients (P<0.05). The nomogram model demonstrated good discrimination, with the area under the ROC curve of 0.775. The Hosmer-Lemeshow showed perfect fitting degree (P=0.395, P>0.05), and the calibration curve approached to the ideal curve. The C-index of 0.782 was reached in internal verification.  
Conclusion: The model developed in this study with 7 predictors has satisfactory predictive efficacy, with good discrimination and calibration, which can provide references for medical staff to early identify high-risk kidney transplantation recipients with IM nonadherence and to formulate relevant intervention measures.  
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P15.08  
Effects of Bcl-6 Inhibition on the Humoral Alloresponse  
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Introduction: BCL6, is a transcription factor involved in B cell activation and differentiation. BCL6-expressing B cells play a crucial role in the development and maintenance of germinal centers, which are essential for the development of a humoral response. Targeting BCL6-mediated responses has the potential to prevent humoral alloreactivity. Here, a small molecule BCL6 inhibitor named 79-6 was tested in vitro and its effect on plasma blast formation and IgG production was investigated.  
Material and Methods: The following experiments were performed in the presence and absence of the small molecule BCL-6 inhibitor 76-9 (range 25-100 µg/mL): (1) Polyclonally-activated B cells (anti-IgM/anti-CD40 and IL-21) from healthy controls were studied for differentiation, plasma cell formation and IgG-production. (2) To study 79-6’s inhibitory effect on B cell differentiation stages, circulating TfH cells and B cells were stimulated with alloantigen, and 79-6 was added at different time points (day 0, 3, and 7).  
Results and discussion: After polyclonal stimulation, a median of 7.4% of the B cells differentiated into plasmablasts. In the presence of 79-6, plasma-blast formation was significantly inhibited by 91% and the proportion of class switched memory B cells dropped by 22%, both p<0.01). Production of IgGs was measured in culture supernatants (median of 600 ng/ml), After inhibition by 79-6, IgG-concentrations were significantly reduced (91%, p <0.01). After stimulation with alloantigen, B cells successfully differentiated into plasma blasts (median 9.8%). Early addition of 79-6 (day 0, day 3) resulted in inhibition of plasma blast formation (median inhibition: 97% and 73%, respectively), while addition of 79-7 at day 7, when B cells have differentiated into plasmablast, did not result in significant inhibition of plasma blast formation.  
Conclusion: 79-6 effectively inhibits differentiation of B lymphocytes into immunoglobulin-producing plasmablasts, whereas it does not inhibit Ig production once plasmablast formation is established. This implies that the timing of 79-6 administration in clinical practice is crucial.
P15.09

**Determination of Tacrolimus Dosage Using Machine Learning in Kidney Transplantation**

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**Introduction:** Maintaining tacrolimus trough levels in kidney transplantation is very important. The purpose of this study is to analyze the determination of tacrolimus dosage to maintain tacrolimus trough levels using machine learning.

**Methods:** This retrospective study included 801 consecutive patients from a prospectively registered database who underwent kidney transplantation at Seoul St. Mary’s Hospital, South Korea, between January 1, 2015 and December 30, 2019. After kidney transplantation, supervised learning was performed based on individual tacrolimus trough levels and tacrolimus dosage during hospitalization.

**Results:** A total of 771 patients were enrolled in the study with a mean age 48.7 ± 11.5 years (range 16 – 75). 445 (57.7%) patients was male. 326 (42.3%) patients was female. 157 (20.4%) was ABO incompatible kidney transplantation. and 196 (25.4%) patients was deceased donor kidney transplantation. Significant results of tacrolimus trough levels and tacrolimus dosage during hospitalization were confirmed through machine learning. It was analyzed that weight had a significant effect.

**Conclusion:** Determination of tacrolimus dosage to maintain appropriate tacrolimus trough levels through machine learning during hospitalization after kidney transplantation should be considered as a useful tool.

**Keywords:** Kidney transplantation, Machine learning, Tacrolimus.

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P15.10


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**Background:** The path of success of kidney transplantation reflects the accuracy of immunological risk assessment and the choice of the correct induction and maintenance immunosuppression to avoid acute kidney rejection.

**Methods:** We performed multicentre prospective analysis consisting of patients after kidney transplantation with 12-month follow-up. The aim of the study was to stratify the immunological risk based on the presence of risk factors using different induction immunosuppressive protocols.

**Results:** 152 kidney transplant recipients were included, 100 males (66.4%). We divided patients according to induction immunosuppression: no induction (n = 19), induction with basiliximab (n = 60), induction with ATG cumulative does 3.5 mg/kg (n = 42) and 6 mg/kg (n = 31). In our study, we demonstrated a shorter survival of patients without induction immunosuppression. In basiliximab group duration of dialysis ≥ 3 years (P = 0.0191), cold ischaemia time ≥ 1020 minutes or expected delayed graft function (P < 0.0001) are independent risk factors for graft loss (P = 0.0097).

**Conclusions:** Risk of no induction immunosuppression significantly exceeds the risks associated with its administration and is desirable even in patients with low immunological risk. Induction immunosuppression should be tailored individually from patient to patient.

Matej Vnučák participated in performing the research and writing the paper.
Karol Graňák participated in writing the paper.
Monika Beliančinová participated in data collection.
Igor Gaňa participated in data collection.
Michaela Chrapeková participated in data collection.
Andrea Kováčová participated in data collection.
Luboslav Beňa participated in performing research.
Zuzana Žilinská participated in performing research.
Ivana Dedinská, PhD. participated in writing the paper, statistical analysis.
P16.01
Decreased Mortality From SARS-coV-2 Infection in Kidney Transplant Recipients Over the Course of the Pandemic

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We aimed to investigate the variation in mortality from SARS-CoV-2 infection in kidney transplant recipients in the Bronx, New York since the beginning of the pandemic. Between March 16, 2020 and March 14, 2022, 499 patients were diagnosed with SARS-CoV-2 infection by RT-PCR. 58.8% were male, median age 59 years old (IQR: 46-67), predominantly Hispanic (50.1%) and African American (28.7%). 74.6% received a deceased-donor renal transplant, 46% received anti-thymocyte induction. Most patients were on triple immunosuppression (96% on calcineurin inhibitors, 87% on anti-metabolite, and 98% on prednisone). While the mortality rate was 57 % (47/129) in patients during first peak between March 16 and April 30, 2020, it has significantly decreased to 11% (7/61) from May 1, 2020 to end of December 2020 with social distancing and use of facemask. Between January 1, 2021 and November 5, 2021 with use of vaccination and monoclonal antibodies, the mortality rate further decreased to 7.7% (10/129). Between November 6, 2021 till March 14, 2022 which corresponds to the period when the Omicron variant was prevalent, the mortality rate was 6.6% (12/181). Among those diagnosed during the period when Omicron was prevalent, 156/181 (86%) have received 2 doses of COVID vaccine and 67/181 (37%) have received a third dose. Mortality was 6.4% in vaccinated patients and 4.7% in non-vaccinated patients. Since the beginning of use of monoclonal antibodies in mild cases not requiring hospitalization, 76 patients received a combination of casirivimab/imdevimab when initial SARS-CoV-2 variants were dominant and sotrovimab during the period of Omicron. Only one death occurred in patients who received monoclonal antibody treatment. We identified a total of 19 re-infections. Most of re-infected patients have already received at least 2 doses of COVID vaccine. 7/19 (37%) were hospitalized but none of them died.

In summary, mortality from SARS-CoV-2 infection in kidney transplant recipients was higher earlier in the pandemic and has significantly decreased over time. This could be explained by initial exposure of the patients with higher viral load due to lack of personal protection and social distancing. However, since the judicious use of monoclonal antibodies and vaccination, in addition to social distancing protocols and use of facemask, the mortality in kidney transplant recipients has decreased over time.

P16.02
Safety and Effectiveness of COVID-19 Vaccination in the Islet Transplant Recipients

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Background: Response to Covid vaccine among transplant recipients remains diminished comparing to general population. Here, we assessed safety and effectiveness of the Covid vaccination in the protection from the Covid infection and in the induction of the SARS-CV-2 Spike total antibody (Spike ab) in islet transplant recipients.

Methods: We analyzed immune response to Covid-19 and COVID-19 vaccination in a cohort of 20 islet transplant recipients: N=13 after islet transplant alone (ITx), N=7 with islet after kidney (IAK) or pancreas after islet graft (PAI). The median age was 48 years (25-62). Maintenance immunosuppression included tacrolimus and an antimetabolite in addition to 5mg of Prednisone in IAK and PAI recipients. Four patients got booster.

Results: Seven patients (38%) chose not to be vaccinated and 5 (71%) of them remained Covid-19 free with no Spike ab present in their blood. The other two patients (29%) had only mild symptoms of COVID-19 infection with Spike ab detected afterwards (46U/ml -IAK and 150U/ml- ITx). In contrast, all remaining 13 patients (62%), who received vaccination: N= 8 Pfizer, N=4 Moderna, N=1 J&J while on immunosuppression for a median of 7 years (0.5-16), remained Covid-19 free based on lack of symptoms and PCR testing (p=0.11, Fischer). The level of Spike ab in response to vaccine varied: undetected- (N=4), range- 5-40U/ml (N=4), range around 75U/ml (N=2), around 400U/ml (N=2), and above 2,500U/ml (N=1). Presence of 5mg of Prednisone did not affect the outcomes. None of the patients experienced moderate/severe adverse events related to the vaccination. Booster administered 4-6 months after the second dose of the vaccine increased the level of Spike ab from 22, 92, 441 to over 2,500 in all 3 patients, respectively. One patient who did not develop any Spike ab after Pfizer vaccine, also did not respond to the booster. Islet graft function remained stable in all patients during 8-12 months after initial vaccination. There were no SAEs related to the vaccination or booster.

Conclusion: One third of unvaccinated islet transplant recipients developed Covid-19, however, all of them presented only with mild symptoms. In contrast, none of vaccinated transplant patients developed COVID-19 infection with 69% rate of seroconversion after vaccination. Booster increased level of the Spike ab in those patients who responded to the original vaccination.
P16.03

Argentine COVID 19 Registry Transplantation: A National Cohort Study

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Introduction: Solid organ transplant recipients may be at increased risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and death; however, epidemiological evidence is lacking in Argentina.

Method: INCUCAI (National Authority of Organ and Tissue Procurement and Transplantation) has carried out a national cohort study, with the aim of knowing the incidence of COVID-19 infection in transplanted patients during the pandemic in the country, analysing prognostic factors and evolution through multivariate analysis. The main source was Information Registry and Management System of Argentina (SINTRA).

Results: We analysed three periods, first: 03/31/20 – 02/28/21, second:03/01/21 – 11/30/21 and third:12/01/21 – 02/28/22 were confirmed COVID-19, 5,324 patients (9% of the total living transplanted patient). Mortality rate was = 20% (310/1549); 20% (384/1892) and 3% (56/1883) for each period respectively. The 72% of the covid confirmed patients are kidney and 16% liver transplantation. The covid confirmed deceased patients are 77% kidney transplantation and 13% liver tx. In the multivariate analysis, transplant patients’ probability of death were associated to patient age, hospitalization, and mechanical ventilation requirement along the tree periods. However, comorbidities like HTA and DBT and waiting list type were unstable associated along the periods to the mortality. Patient gender and smoker are not associate to mortality.

Conclusion: In conclusion, patients on the waiting list and transplanted patients have a higher probability of COVID infection and worse evolution than the general population. Transplant patients have a lower incidence and better evolution of COVID-19 infection than patients on waiting lists.

P16.04

Seroprevalence of SARS-CoV-2 Antibodies Following Vaccination Amongst Renal Transplant Recipients: A Single Centre-Experience

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Aims: Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) poses significant increased mortality in patients undergoing solid organ transplantation. Several vaccines have emerged attempting to mitigate the effects of SARS-CoV-2 amongst vulnerable patient cohorts. This study evaluated the seroconversion rate to SARS-CoV-2 vaccination and antibody persistence following renal transplantation and commencing immunosuppression therapies.

Methods: 39 patients received a renal transplant between 17/03/21 – 18/11/21. All patients received 2 doses of Pfizer-BioNTech (BNT162b2) or Oxford/AstraZeneca (AZD1222) vaccination prior to renal transplant. Serum antibodies were tested for pre renal transplant. Further antibody tests were performed at 1 and 3 months respectively.

Results: The mean recipient age was 48.1 years (range 18-74 years). All recipients received the second vaccine dose at least 6 weeks pre-transplant. Serum antibody persistent was best appreciated following the Pfizer-BioNTech vaccination (100% at 3 months). Comparatively, diminished antibody response was observed in recipients receiving the Oxford/AstraZeneca vaccine (84% at 3 months). Of the four non-responders post Oxford/AstraZeneca vaccination, 2 had failing transplants (on IS). One recipient developed antibodies at 1 month following the Oxford/AstraZeneca regimen: This may have been secondary to natural exposure or an initial false negative result. There were no acute SARS-CoV-2 infections amongst the cohort. No adverse vaccine-related outcomes were observed.

Conclusions: This study suggests vaccination is an effective measure for obtaining SARS-CoV-2 serum antibodies amongst pre-transplant patients. Limited data suggests that pre-existing IS may be an inhibitory factor in relation to vaccination efficacy. Higher seroconversion rates were observed following Pfizer-BioNTech vaccination. Larger scale studies over longer periods are required to investigate antibody persistent in such patients.
Adaptive Strategies Implemented by an OPO in Argentina For the Protection of Transplant Patients and the OPO’s Own Staff in the Context of the SARS-CoV-2 Pandemic

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Introduction: The SARS-CoV-2 Pandemic has been a threat to human health, but specially for transplant patients, who are immunosuppressed, as the virus could increase the case-fatality rate among them. Because of this, strict home confinement was recommended for transplant patients in 2020 and 2021. In this context, the Transplant Institute of the City of Buenos Aires (EAIT), Argentina, developed a series of strategies to mitigate the negative impact caused by the confinement. The two core measures were implemented by the Pharmacy and Psychosocial Areas.

Method: Descriptive, cross-sectional, observational, and retrospective design. The strategies were monitored through anonymous surveys using the Google Forms platform, WhatsApp messages, and calls. The Pharmacy Area created a medicine delivery and pharmacotherapeutic follow-up system for transplant patients under the public healthcare system, to whom the State supplies immunosuppressive drugs for free. The Psychosocial Area held supporting meetings, and virtual workshops, and made arrangements for patients and families.

Results: Pharmacy Area: Total number of consultations: 3110. Average number of consultations per patient: 15.32. Problems solved: 93.8% (2917). Patients under active monitoring: 59.89% (109). Consultations via WhatsApp: 0.13% (3). Classification: Patient Follow-up 45.4% (219). Therapeutic drug confirmation: 13.7% (66). Dose adjustment/ change of medication: 6.8% (33). Consultations related to COVID-19: 6.2% (30). Pharmaceutical consultations: 2.5% (12). Patients admitted to the Argentine Healthcare State Program (PNSP): 2.1% (10). Miscellaneous consultations: 23.3% (112). Satisfaction survey: In relation to drug delivery service quality, 98.1% (157) of respondents stated that they received the medicines at home correctly, rating home delivery system with 8/10 or higher. As to the ease of communication with pharmacists, 94.4% (152) of respondents stated that they found it easy to communicate with pharmacists over the quarantine. In terms of problem solving, 91.8% (146) of respondents stated that they could solve their problems. As to the attention received, 99.4% (157) rated it as good and very good. Psychosocial Area: Virtual meetings:340; calls:3970; attention to patients admitted to the Argentine Healthcare State Program (PNSP): 2.1% (10). Miscellaneous consultations: 23.3% (112). Satisfaction survey: In relation to drug delivery service quality, 98.1% (157) of respondents stated that they received the medicines at home correctly, rating home delivery system with 8/10 or higher. As to the ease of communication with pharmacists, 94.4% (152) of respondents stated that they found it easy to communicate with pharmacists over the quarantine. In terms of problem solving, 91.8% (146) of respondents stated that they could solve their problems. As to the attention received, 99.4% (157) rated it as good and very good.

Findings: Within a context in which a sense of fear, anguish, and uncertainty prevailed, the rapid response from the EAIT -through the implementation of proper strategies- succeeded in keeping the negative impact of confinement on this vulnerable group and the institutional healthcare team to the minimum, besides having a very high degree of satisfaction.

Seroconversion in Patients After SARS-Cov-2 CHADOX1 NCoV-19/AZD1222 Vaccination in Hemodialysis Patients And Kidney Transplant Recipients

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Background: Since December 2019 the world has been affected for Coronavirus SARS-CoV-2 pandemic. In Aguascalientes state at March 13th 2022 has been confirmed a total of 62,440 cases and 3,479 deaths caused by COVID-19. As a combat strategy were developed different kind of vaccines against SARS-CoV-2. The Oxford University developed the vaccine ChAdOx1 nCov-19/AZD1222 which is based in a viral vector which codes the information of the spike protein of SARS-CoV-2. It has been proven that the morbidity and mortality from COVID-19 is higher in hemodialysis (HD) patients and Kidney Transplant (KT) recipients.

Objective: Measure and compare the seroconversion level in hemodialysis patients and kidney transplant recipients (KTR), who received two doses of the ChAdOx1 nCov-19/AZD1222 vaccine and identify the factors associated with low response to the vaccine used in our study population.

Methods: We performed a prospective, observational, unblinded and comparative analysis. Patients included between 18-80 years old, both genders, that they were in HD or with KTR, and received two doses of the ChAdOx1 nCov-19/AZD1222 vaccine between 2-6 months before sampling. The antibodies level against spike protein of SARS-CoV-2 was determined by the immunoasay Elecsys anti-SARS-CoV-2 and we determined a positive result ≥100 U/mL.

Statistical Analysis: iChi² test with Yates’ correction, Student’s T-Test with low response to the vaccine used in our study population. p<0.05 was considered as significant.

Results: 67 patients were included, 49 in HD and 18 with KTR. In the multiple logistic regression analysis, taking the positive seroconversion ≥100U/mL as the dependent variable, the KT was the risk factor associated with a lower seroconversion frequency, p<0.05 Exp(B) 3.26.

Conclusions: The ChAdOx1 nCov-19/AZD1222 vaccine was associated with a higher seroconversion level in HD patients in comparison to KTR. The KTR patients presented a higher frequency of SARS-CoV-2 infection post vaccination in relation to HD patients. The main risk factor associated with lower seroconversion response was KT in patients who received the ChAdOx1 nCov-19/AZD1222 vaccine. Our population presented a higher seroconversion response that reported in the literature, probably because of the SARS-COV2 infection antecedent prior to vaccination.
Association Between SARS-CoV-2 Infection and de Novo HLA Donor Specific Antibody Production in Lung Transplant Recipients: Single-Center Study

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Introduction: COVID-19 pandemic has led to significant morbidity and mortality in lung transplant recipients. Respiratory viral infections may be associated with de-novo HLA donor specific antibody production and impacting lung transplant outcome.

Methods: Since one of the immunomodulation strategies post-SARS-CoV-2 infection in lung transplant recipients include decreasing or holding anti-metabolites, concerns have been raised for higher incidence of de-novo HLA donor specific antibody production in lung transplant recipients. We performed a retrospective chart review of 24 consecutive lung transplant recipients diagnosed with COVID-19 to investigate this concern.

Results: We observed no significant association between SARS-CoV-2 infection and immunomodulation on pre-existing or de novo HLA donor specific antibodies.

Conclusion: SARS-CoV-2 infection was not associated with a significant increase in de-novo HLA DSA production or MFI levels of pre-existing HLA DSA compared to pre-COVID-19 diagnosis in lung transplant recipients. These results provide a valuable insight on the effects of SARS-CoV-2 infection on immunogenicity in lung transplant recipients.
COVID-19 Positive Kidney Transplant Recipients Behave Differently Compared to Non-transplant Patients ICU: Single Center Experience

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Introduction: COVID-19 is an ongoing pandemic that has altered our lives especially that of kidney transplant recipients (KTR).

Aim: We aimed to compare COVID-19 positive kidney transplant recipients with non-transplant positive cases that were managed in the intensive care unit (ICU) during the pandemic.

Methods: Out of 2000 KTR that was followed up in Hamed Al-Essa Organ transplant center in Kuwait, we collected data of all COVID-19-positive KTR (group 1, n=79) till the end of January 2021. Clinical features, management details, and both patient and renal outcomes were reported and compared with (group 2, n=445) non-transplant cases admitted during the same period in the ICU of a single isolation hospital in Kuwait during the pandemic.

Results: Most of the cases were males (74% vs.73%), aged 51.7±16 and 60.8± 14 years in the 2 groups respectively. Both groups were comparable regarding patients with diabetes mellitus (50.6 vs. 55.2%), hypertension (62% vs 57.1%), ischemic heart disease (20% vs 19.8%) and chronic kidney disease (1.3% vs 1.6%). Fever, cough, body aches, and gastrointestinal symptoms were the most frequent presentation among KTR. Meanwhile, complicated cases with sepsis, volume depletion, shock, and ARDS predominated among the non-transplant group (p<0.05). Therapeutic management included anticoagulation (81 %) in both groups, while steroid and tocilizumab were used frequently among the non-transplant group (8.7%). Within 30 days follow up, the non-transplant group showed a significantly higher number of cases with acute kidney injury (47.8% vs. 26.7%), respiratory failure requiring mechanical ventilation, and mortality rate (54.4% vs. 22.8%).

Conclusion: we reported a better outcome of ICU admitted COVID-19 positive KTR in comparison with the non-transplant patients possibly due to younger age modified immunosuppression.

Spectrum of Side Effects of mRNA COVID-19 Vaccine Among Asian Kidney Transplant Recipients and Healthcare Providers At the Singapore General Hospital

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Background: In Asia, COVID-19 vaccine hesitancy among solid organ transplant recipients has been reported to be as high as 77.2%. There is lack of data addressing the side effect profile of mRNA vaccine in Asian transplant recipients which is important, given that reassuring data may reduce vaccine hesitancy. As a result, this study compares the spectrum of side effects observed with 2 doses of mRNA vaccine in kidney transplant recipients (KTX) and healthcare providers (HP) from the Department of Renal Medicine at the Singapore General Hospital.

Methods: A cross-sectional survey was conducted via an online questionnaire for a period of 3 months. The questionnaire collected data on demographics, previous vaccine uptake history, type of vaccine received, side effects observed and post-vaccination sequelae like outpatient/inpatient medical attendances and COVID-19 infection.

Results: The study population consisted of 120 KTX and 96 HP, all receiving 2 doses of mRNA COVID-19 vaccine but more HP than KTX had received their vaccine more than 2 months ago (89.6% vs. 67.7%; p<0.005). The proportion of KTX and HP experiencing side effects from their 1st dose was similar (77.4% and 84.4% respectfully; p=0.197) but the proportion of KTX experiencing side effects from their 2nd dose was lower than compared to HP (75%; vs. 89.6%; p=0.008). For the first dose and second dose, the number of side effects reported was also lower among KTX compared to HP (1.44±1.42 vs. 2.31±2.0; p=0.005 for the 1st dose and 1.38±1.33 vs. 2.91±2.4; p<0.005 for the 2nd dose) and more KTX reported no or mild side effects compared to HP (89.4% vs. 79.1%; p<0.005 for the 1st dose and 92.3% vs. 65.6% for the 2nd dose; p=0.005). Compared to HP, less KTX experienced swelling (8.1% vs. 28.1%; p<0.005 for 1st dose and 8.1% vs. 33.3%; p=0.005 for 2nd dose), injection site redness (5.2% vs. 10.4%; p=0.03 for 1st dose and 2.4% vs. 10.4%; p=0.031 for 2nd dose), body ache (15.3% vs. 32.3%; p<0.005 for 1st dose and 14.5% vs. 38.5%; p<0.005 for 2nd dose), chills (0.8% vs. 8.3%; p=0.005 for 1st dose and 4.8% vs. 16.7%; p=0.011 for 2nd dose) and headache (6.5% vs. 14.6%; n=0.046 for 1st dose and 7.3% vs. 20.8%; p<0.005 for 2nd dose). In addition for the 2nd dose, less KTX experienced fever (7.3% vs. 27.1%; p<0.005), giddiness (0.8% vs 7.3%; p=0.027) and arthralgia (1.6% vs. 8.3%; p=0.042). A lower proportion of KTX compared to HP also needed to see a doctor following vaccination (2.4% vs. 6.3%; p<0.005 for the 1st dose and 1.6% vs. 14.5%; p<0.005). There were 2 cases of post-vaccination Bell Palsy among KTX and 1 KTX suffered rejection after 2 dose of vaccine.

Conclusion: Contrary to patients’ perceptions, side effects from COVID-19 mRNA vaccine are none or mild in the majority of KTX receiving these vaccines. Serious side effects like Bell Palsy and rejection were rare. Interestingly, side effects were less common among KTX than HP, presumably because immunosuppression blunted the side effects in KTX.
SARS-CoV-2 Vaccination in Liver Transplant Recipients

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Introduction: Some previous research suggests that a protective immune response after vaccination is diminished in kidney transplant recipients. The literature in other types of solid organ transplant is even scarcer. With the development of the SARS-CoV-2 vaccines, there was fear that transplant recipients would not mount a sufficient response to vaccination. We sought to evaluate the antibody response of liver transplant recipients to SARS-CoV-2 vaccination, especially in liver transplant recipients. Various guidelines suggest transplant recipients should be vaccinated, and are eligible for additional doses in cases with an inadequate response.

Methods: During routine follow up of 262 liver transplant recipients (earliest date of transplant 1998) at Universitätsklinikum Graz we gathered the information about their vaccination status. As part of routine follow up, we also determined the serum concentrations of SARS-CoV-2 antibodies.

Results: Of the 262 patients in follow up, we currently have the vaccination details of 128 who received at least one vaccine dose. 2 patients received an initial two doses of a vector vaccine, all other doses were of an mRNA vaccine. Of the 127 patients who were vaccinated at least twice, 107 achieved an excellent response (>100U/mL) and 7 achieved an adequate response (>=30U/mL). Of the 13 patients who achieved an inadequate response (<30U/mL), 6 had no detectable circulating antibodies. Of the 115 patients who were vaccinated at least three times, 101 achieved an excellent response and a further 6 adequate. 8 patients still did not achieve an adequate response after vaccination (<30U/mL), 6 had no detectable circulating antibodies. Of the 115 patients who were vaccinated at least three times, 101 achieved an excellent response (>=30U/mL), 6 had no detectable circulating antibodies. Of the 115 patients who were vaccinated at least three times, 101 achieved an excellent response (>=30U/mL).

Conclusion: After at least two vaccine doses, 89.8% (114/127) of patients had an adequate response to the vaccine. After the third dose, the response rate rose slightly to 93.0% (107/115). The currently available vaccines appear to provoke a sufficient antibody response in liver transplant recipients.

Decreased Immunogenicity After SARS-CoV-2 Vaccination in Liver and Kidney Transplant Recipients

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Background: Recently published studies have found an impaired immune response after SARS-CoV-2 vaccination in solid organ recipients. Most of these studies have not assessed immune cellular responses in solid organ transplant recipients. And no studies have yet demonstrated the efficacy of a booster (third) dose of SARS-CoV-2 vaccination in these patients. In this study, a prospective double-arm cohort study was performed to evaluate the humoral and the cellular immune response to SARS-CoV-2 vaccination in solid organ transplant recipients compared to healthy staff members with the normal function of the immune system.

Methods: A total of 64 transplant patients and an age-matched control group of 103 healthy staff members were included. Blood samples were obtained and analyzed after the second dose and the boosting (third) dose, respectively. For evaluation of the virus-neutralization capacity of each group, serum was analyzed using a surrogate SARS-CoV-2 neutralization test to quantify the functional inhibitory capacity of neutralizing antibodies against SARS-CoV-2 spike protein. Inhibition scores of under 30% was considered negative.

Results: Except the vaccination subgroup of the initial two dosages of AstraZeneca followed by Pfizer was significantly higher in the healthy control group, another prime-booster combination subgroup proportions were similar between the group. After the standard two doses of vaccination, only 28.3% of the transplant recipients demonstrated positive functional inhibition of neutralizing antibodies, significantly lower than 70.9% of the healthy control group (p <0.001). Even after the booster (third) dose of vaccination, 43.2% of the transplant recipients showed positive functional inhibition of neutralizing antibodies, significantly lower than 100% of the healthy control group (p <0.001). No other immune-associated complications such as acute rejection has occurred after SARS-CoV-2 vaccination in the transplant recipient group.

Conclusion: Our data strongly suggest revised vaccination approaches in immunocompromised patients, including individual immune monitoring for the protection of this vulnerable group at risk of developing severe COVID-19. It urges for a review of future vaccine strategies in these patients.
Introduction: Novel coronavirus disease (COVID-19) is a newly discovered contagious contagious disease caused by SARS-CoV-2 virus, primarily manifesting as an acute respiratory illness with pneumonia, but can affect multiple organs such as kidney, heart, digestive tract, blood and nervous system. Patients with end-stage kidney disease undergoing dialysis or kidney transplant recipients are particularly vulnerable to severe COVID-19 due to the older age and high frequency of comorbidity, such as diabetes and hypertension, in this population. Reported mortality is higher than usual annual mortality and is associated with older age and number of comorbidities. Despite two years of pandemic data are still limited in relation to three modalities of renal replacement therapy in Poland.

Methods: Retrospectively collected data in single university hospital on hemodialysis, peritoneal dialysis and kidney transplant recipients engrafted during pandemic. We viewed epidemiologic and clinical data of patients with laboratory-confirmed COVID-19 and assess mortality in 2019, and 2020 and 2021.

Results: Unadjusted mortality in dialyzed patients (number of deaths divided by number of patients) in 2019 was 19%, while unadjusted (after exclusion of COVID-related deaths) mortality in 2020 was 21%, in 2021 mortality was 25%. The prevalence of cardiovascular deaths in 2019 and 2020 and 2021 was almost identical (41 vs 41 vs 42%). In kidney transplant recipients mortality in 2019 was 3%, in 2020 was 3% (COVID-19 related) and in 2021 was 7% (all COVID19 related). Mortality of COVID-19 positive dialyzed patients contributed to the 24% of all recorded deaths.

Conclusions: Patients receiving maintenance hemodialysis were susceptible to COVID-19 and that hemodialysis centers were high- risk settings during the epidemic. However, changes in the HD schemes due to necessity to isolate COVID-19 positive patients, shortened dialyses did not change significantly of the cardiovascular mortality in dialyzed population. COVID-19 is a huge challenge and danger for dialyzed population. Kidney transplant recipients despite immunosuppression were less vulnerable.
P16.14
Impact of Vaccination Against COVID 19 in the Population of Intrathoracic Transplant Recipients During the Pandemic

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Introduction: Towards the end of 2019, the SARS CoV-2 infection was reported in the Chinese city of Wuhan, which gave rise to the current pandemic. In the presence of an immunosuppressed patient, the clinical picture is undoubtedly variable, and therapeutic and preventive tools take an important role. The objective is to present the experience in patients with intrathoracic transplant.

Methods: Observational, retrospective study in orthotopic, single-lung, double-lung, and cardiopulmonary heart transplant patients under follow-up at Hospital Italiano de Mendoza, Argentina, from August 2020 to February 2022, with a positive PCR diagnosis or symptomatic epidemiological link for COVID 19.

Results: A total of 37 patients were included, with a mean age of 58.2 years (16 to 76 years), 89% were orthotopic heart transplant recipients, 3% single-lung, 3% double-lung, and 3% heart-lung. During the first wave between March 2020 and November 2020, in the national context of mandatory quarantine, there were 8 infected with moderate-severe symptoms in 4 patients and a mortality of 37.5%. During the second wave (May 2021), vaccination began in immunosuppressed patients, in this context there were 13 infected, 62.5% with severe symptoms, with a mortality of 38.4%, 69% of vaccinated with at least one dose. At the beginning of 2022, with the advanced vaccination campaign, the cases in our country increased exponentially, 16 patients were infected. 100% were vaccinated. In this context, of the 8 who received 2 doses of the vaccine prior to contracting the disease, 3 had moderate-severe symptoms. Only 5 patients managed to complete the vaccination schedule with 3 doses, and no severe symptoms were observed in this subgroup. Finally, the mortality of the third wave was 12.5%.

Conclusion: In our population, we observed that as the pandemic progressed, the number of infections increased, but the appearance of immunization made a difference in terms of morbidity and mortality, surely also associated with the lower virulence of the strains that predominated in our country in each of the three COVID-19 waves.

P16.15
HLA Genetic Frequency in Renal Transplantation Patients, Dead by COVID-19

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Introduction: Are well known the HLA associations with diseases, i.e. ankylosing spondylitis with HLA B*27, and some virus and tumors capability to use some strategies for downregulate the HLA molecules expression and to scape the recognition from T lymphocytes. The intention of this work was to analyze probable genetic associations of the HLA Histocompatibility System in patients with a functioning kidney transplant who died of covid-19.

Method: 60 patients (360 genes) from the province of Buenos Aires, Argentina, with a functioning kidney transplant for months/years, both genders, adults, from the CRAI Sur and CRAI Norte kidney transplant centers in CUCAIBA, who died of covid-19 (strain undetermined), and due to short-term complications of covid-19 that are public knowledge. The investigation of gene pairs (maternal and paternal inherited) of the HLA System was done by molecular biology SSP and SSO-Luminex, in low resolution, for HLA Class I: A* A* and B*B* and Class II: DRB1*DRB1* genes. For comparison with the healthy Argentine control population, by NGS molecular biology typing, data were obtained for the same genes and taken from high to low resolution, from 2657 people (15942 genes) from all over the country, also of both genders and adults. This data were obtained from the INCUCAI CPH Donor Registry, data that had already been previously presented at the 2014 congress in Buenos Aires and published in Transplantation Proceedings, 46, 3064-3067, in 2014.

Results: We observed the following variations in the gene frequency of death patients respect to healthy population (Control): see table 1. Additional data will be added to the final work.

Conclusion: The purpose of this work was to investigate whether any of the HLA genes mentioned, present in kidney transplant patients who died of covid-19, predisposed to the outcome of the disease, or whether genes not present in this population (whose frequency is observable in a healthy population), were able to protect the population of kidney transplant patients who did not die from covid-19, a population that will be analyzed in the future.

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Seroconversion in Liver and Intestine Transplant Patients After One, Two or Three Doses of Adenoviral Vector Vaccines Against SARS-CoV-2. Single Center Experience in Argentina

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Introduction: The capacity of different anti-SARS-CoV-2 vaccines to elicit immune response is not equivalent in the healthy population compared to chronically immunosuppressed patients. Most of the reports available so far to assess the effects of anti-SARS-CoV-2 vaccines on solid organ transplant recipients (SOTR) were performed using mRNA-based vaccines. The majority of the vaccines used so far in our country are adenovirus-vector vaccines (Sputnik V and Covishield/AstraZeneca-Oxford). Goal: to assess the seroconversion after vaccination with the non-replicative vector-based vaccines after transplantation.

Methods: Seventy-nine patients of liver transplant (79), combined liver-intestine transplant (1) or intestinal/multivisceral transplant (4) receiving their first vaccine dose between March and June 2021 were included, mean age of was 55.6 years old (range 18-75.9; 71% males). All patients have a post-transplant follow up longer than 1 year (median 6 years, range 1-25 years). Samples after second and third doses were also analyzed, in all cases obtained at least three weeks after last vaccination. Patients serological status was evaluated using three different anti-S commercial ELISA kits and an in-house made anti-N ELISA. Patients with previous PCR-confirmed COVID19 were excluded.

Results: We found that 28.1% of patients (9 out of 32) seroconverted after a single dose of Sputnik V (8 out of 21) or Covishield (1 out of 11), whereas 18 out of 27 (66.7%) seroconverted after second dose of Sputnik V (7 out of 10) or Covishield (11 out of 17) and 12 out of 13 seroconverted after a third dose (92%), most of them have received two doses of Sputnik V and receiving Moderna, Pfizer or Covishield as third dose. There is a significant difference in the proportion of seroconversion between the groups that received one dose or two doses of vaccine (p<0.005, Chi square test) whereas the difference is not significant between groups receiving two and three doses (p=0.08, Chi square test). The comparison between responder’s and non-responders to the single dose vaccine showed no differences in either patient age, post-transplant time, days after vaccination, presence of comorbidities and maintenance immunosuppressive therapy.

Conclusion: Despite having a lower seroconversion rate compared to the general population, viral-vector vaccines benefit SOTR patients increasing the seroconversion rate using at least two doses of vaccine. These results support the concept of developing tailor-made vaccination guidelines for this specific population.
P16.18

Behavior of Anti-SARS-CoV-2 Antibodies in Renal Transplant Patients Vaccinated Prior to Transplantation

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Introduction: Renal transplant patients develop a decreased antibody response to COVID-19 vaccines compared to patients on dialysis. Antibody titers are expected to decline over time. There is little information on the behavior of these titers in patients with a significant immunosuppressive load, such as transplant recipients. This paper aims at describing the behavior of anti-SARS-CoV-2 antibodies in a group of patients vaccinated while on dialysis who received a kidney transplant, and at comparing them with a group of patients who continued on hemodialysis.

Methods: For dialysis patients receiving a deceased donor kidney, on the transplantation day and before starting the immunosuppressive therapy, anti-SARS-CoV-2 antibodies were measured and measured once again 2 months after transplantation on average. Patients who were and continue to be on hemodialysis were used as a control group. Their antibodies were measured at the same moments as those for transplant recipients.

Results: Sixteen patients were evaluated, 8 were renal transplant patients (RTPs) and 8 were patients on dialysis (HDPs). The gender distribution was 13 men in total (7 RTPs and 6 HDPs). Average age was 42±14 and the length of time on dialysis for RTPs was 4.8±3 years, with no difference between RTPs and HDPs. In RTPs, baseline antibodies were first measured (prior to transplantation) 97 days (69-133) after the second dose and were measured once again 76 days (44-103) after transplantation, i.e. 173 days after the second dose and 28 days after the third dose. In the HD group, baseline antibodies were measured 40 days after the second dose and were measured once again 120 days after the second dose and 84 days after the third one. In RTPs antibody titers were 3.61±0.25 prior to transplantation and 3.12±1.2 following transplantation, with no significant differences between the pre- and post-transplant periods (p=0.3). It should be noted that 5 out of the 8 patients had received a third dose of the vaccine. In HDPs, no significant differences were found either when comparing the titers of baseline antibodies and those of the second measurement (3.37±0.02 vs. 3.64±1.2 P=0.5). When comparing the antibody variation in the first and second measurements, a decline of 0.05±1.84 in RTPs and an increase of 0.26±1.2 in HDPs were found, with no statistically significant differences. All RTPs have a stable kidney function and do not require dialysis.

Conclusion: While RTPs showed a decline in antibody titers and HDPs, a slight increase in titers, no differences between baseline and subsequent determinations or between both groups were found. Further studies are required to assess the effects of immunosuppression and whether it makes this population more susceptible to SARS-CoV-2 infection.

P16.19

Omicron COVID-19 in Kidney Transplant Recipients

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Introduction: In Brazil covid-19 caused more than 22 millions cases and 600 thousands of COVID-19 related deaths at the end of the second year. In 2022 the Omicron variant wave caused millions of cases worldwide and 7.4 million reported cases by March 23 in Brazil. This last variant is associated with a high infectivity and evasion from immune response, but less severe disease and hospitalization compared to previous variants. The better outcome is probably due to lower pathogenicity and immunization rates in 2022. However, reported data have shown that kidney transplant recipients (KTR) remain as a vulnerable group associated with worse outcome. The aim of this study is to evaluate the clinical presentation and outcome of covid-19 among hospitalized KTR with COVID-19.

Methods: We performed a retrospective description of 297 KTR with confirmed COVID-19 pneumonia by positive real-time reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 in a respiratory specimen (n = 289 patients); or positive antigen test (n = 8 patients). The patients were hospitalized in a tertiary university public hospital in São Paulo metropolitan city from the beginning of the pandemic - March 2020 until February 2022. Periods were defined according to epidemiological surveillance of cases, and the three well-characterized periods also overlap with predominant variants circulation in Brazil. The first period represents Wuhan variant, the second period Gama and Delta variants and the third and last period Omicron variant. Baseline characteristics, management, and outcomes were stratified by periods.

Results: The baseline characteristics are similar between the three periods. In the third period more than half of the cohort had already completed immunization (62.7%). Cough, dyspnea, and fever were the most common presenting symptoms through the three periods. Although there was no statistical significance, there is a trend to less respiratory symptoms and fever at hospital admission in the third period and more atypical clinical presentations such as diarrhea. Also, we found a statistically significant longer time until patient admission at the hospital. ICU hospitalization reduced with statistical significance over time as well as there was a downward trend in death rate. However, among patients admitted to ICU, the mortality rates are similar through the study. In the multivariate analysis, age, creatinine at hospital admission and multiple comorbidities are associated with higher risk of mortality, as complete immunization was a protector factor for mortality.

Conclusion: KTR with COVID-19 caused by omicron apparently were admitted with a longer duration of illness, less pronounced symptoms, and lower ICU hospitalization rates. However, among those admitted to ICU, the mortality rates are similar independent of the study period. Complete immunization was associated with lower mortality risk.
Solid Organ Post-transplant Lymphoproliferative Disorders (ptld). Experience of a Center

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Introduction: Post-transplant lymphoproliferative disorders (PTLD) are a serious complication after solid organ transplantation as result of uncontrolled proliferation of B cells due to impaired immune surveillance. It consists of a disease spectrum ranging from benign hyperplasia to aggressive monoclonal forms. Incidence varies between 2 -20%. Risk factors include EBV virus infection status, drugs and time of immunosuppressive therapy. The first step of treatment is reduction the immunosuppression. We analyze our experience to determine the prevalence of PTLD in solid organ transplant patients, show their clinical characteristics, therapy and outcome.

Methods: We retrospectively analyzed the medical records of all adult patients who received a solid organ transplant, diagnosed with PTLD from March 1994 to January 2022 at our institution. Statistical analysis was performed with IBM SPSS program.

Results: Of a total of 3197 transplant recipients, PTLD was diagnosed in 42 (1.3%) patients: cardiac transplantation 4%, liver 1%, lung 1.3 %, renal 0.5%. There were no cases of PTLD in intestinal transplant recipients. Mainly observed in males (78%), median age 55 years. Late PTLD was observed in 85% of patients, with extranodal involvement (71%) and stages III-IV (according to Ann Arbor classification). 11% showed bone marrow involvement. EBV –CMV serology were positive in 66% and 69% respectively. History of at least one transplant rejection prior to PTLD was observed in 50% of cases. 7% of PTLD were classified as polymorphic and 93% as monomorphic disorders including these histological diagnoses: 76% diffuse large b-cell lymphoma, 8% Burkitt’s lymphoma, 5% MALT lymphoma. Anaplastic B lymphoma, Waldestrom disease and lymphocytic lymphoma showed an incidence of 3% each. Regarding treatment, 33% underwent chemotherapy, 26% only rituximab, 7% radiotherapy, 5% surgical resection, 10% patients only reduced immunosuppression regimens and 19% did not receive treatment. 52% achieved complete remission, 7% partial remission and 21% showed no response. Currently 36% of patients are in follow-up, 52% died and 12% were lost in the follow up.

Conclusion:
□The prevalence of PTLD in our centre was 1.3%, in accordance with most of the series reported. □Male gender, extranodal involvement and positive serology for EBV and CMV are the more frequent characteristics among our patients. □Most of PTLD were classified as monomorphic B-cell disorders, Diffuse Large B-cell Lymphoma predominated. □52% of patients achieved complete remission with first line treatment and currently 59% of these are under follow-up. □Although this pathology is rare and with high mortality, early diagnosis is of great importance to improve its prognosis and evolution.

TABLE 2. MULTIVARIATED ANALYSIS: FACTORS ASSOCIATED WITH DEATH

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.07</td>
<td>1.05-1.1</td>
<td>0.000</td>
</tr>
<tr>
<td>Creatinine at Diagnosis</td>
<td>1.25</td>
<td>1.11-1.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Time Period</td>
<td>1.11</td>
<td>0.72-1.7</td>
<td>0.632</td>
</tr>
<tr>
<td>Multiple Comorbidities</td>
<td>1.07</td>
<td>0.62-1.8</td>
<td>0.801</td>
</tr>
<tr>
<td>Completed Immunization</td>
<td>0.3</td>
<td>0.11-0.8</td>
<td>0.015</td>
</tr>
</tbody>
</table>
**P16.21**

**Impact of Vaccination Against SARS-CoV-2 in Kidney Transplant Recipients**

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Introduction: To assess whether vaccination against SARS-CoV2 in kidney transplant patients has an effect in reducing mortality and the severity of coronavirus infection.

Methods: All kidney transplant patients diagnosed with COVID 19 in follow-up by our unit between March 2020 and February 28, 2022 were considered. Severity and mortality from COVID 19 were evaluated according to whether they had received or not vaccination against SARS-CoV2 and also if they received one, two or three doses. The severity of the cases was classified as mild (outpatient management) or severe (hospitalization in a critical unit or death of the patient). Only a small percentage received RNA-type vaccines and a single dose, in combination with others. Age, sex, time since transplantation, time on dialysis of affected patients were analyzed, analysis was performed using Student’s test or Chi square, as appropriate. A value of p<0.05 was considered significant.

Results: Between March 2020 and February 28, 2022, 195 cases of COVID 19 were diagnosed. As of November 2021, a third dose of vaccine was available. No significant differences were observed between the groups regarding age, time on dialysis, female gender, or time since transplant (Table 1). A numerical decrease in mortality was observed depending on whether or not they had received any dose of vaccine, greater in the group that received three doses over those who did not receive any, but statistical significance was not reached (p 0.08). Regarding severity, a higher proportion of mild cases was observed in those who received two and three doses than those who did not receive any (Desp value 0.02) and 0.006 respectively. Given the heterogeneity of the vaccination schedules that included a combination of inactivated virus vaccines (Sinopharm®), DNA vaccines (Astra Zeneca® and Gamaleya®) and RNA vaccines (Pfizer®, Moderna®) and the small number of patients, no was able to discriminate efficacy according to the type of vaccine received.

Conclusion: In the group of patients who contracted COVID 19 and had received three doses of vaccine, a 50% reduction in mortality was observed, although it did not reach statistical significance, probably related to the low number of patients evaluated. Despite this, mortality in this group continues to be very high (14%). It must be taken into account that the patients with three doses who contracted the infection predominantly did so during the circulation phase of the Omicron strain, which is probably less aggressive. A significant increase was observed in the proportion of mild cases among those patients who had received at least two doses of the vaccine. Given the marked heterogeneity of vaccination schedules in our country, added to the small number of cases in each group, no conclusions could be drawn regarding the different types of vaccines available. These results encourage to vaccinate this group of patients and to evaluate the need for a fourth dose.

Sra. Gabriela Melchior.

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**P16.22**

**Graft and Patients’ Outcome in Kidney and Simultaneous Liver-Kidney Transplantation With Infection Control Measures And Immune Suppression Adjustment During COVID-19 Era**

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1Nephrology and transplantation department, faculty of medicine Ain Shams University, Cairo, Egypt.

Introduction: Polices and precautions against Coronavirus disease of 2019 (COVID-19) before and after kidney transplants are highly warranted and modification of induction protocols may reduce the risk of infection. This study assessed the efficacy of COVID-19 prevention protocol with modification of induction at the time of transplantation and maintenance immune suppression during infection on renal graft and patient’s outcome in the first 3-9 months post-kidney transplant.

Method: This Study examined 24 patients who underwent live-related kidney transplantation including one simultaneous liver-kidney transplant from June 2020 to April 2021 after application of our hospital transplantation management protocol during the COVID-19 pandemic. Low to standard risk transplant recipients received ATG 3mg/kg total dose over 4 days and high-risk recipients received 4.5 to 6mg/kg total dose over 4 days.

Results: The patient’s immunological background was human leucocytic antigen (HLA) mismatched in 83.3% (20 patients) ranging from 3 mismatched alleles. Panel Reactive Antibody (PRA) was positive in 41.6% (10 patients), 16.6% (4 patients) had Donor-Specific Antibody (DSA) means SD (2956.12±1361.5) MFI. CDC crossmatch was negative in all patients. COVID-19 infection was detected by polymerase chain reaction (PCR) post-transplant in 16.6% (4 patients). 12.5% (3 patients) had got an infection with mild to moderate symptoms, and 8.3% (2 patients) had rising serum creatinine (2-2.5mg/dl), 4.16% (1 patient) had 2 infection episodes. 1st episode was asymptomatic and the 2nd was moderate symptoms (fever, mild pulmonary ground-glass opacity, and not needing oxygen support). Timing of post-transplant covid-19 infection was in the 8th to 9th week in 12.5% (3 patients) and 24 weeks in 4.16% (1 patient) with negative seroconversion 10-14 days and after 4 weeks of the diagnosis respectively. COVID-19 outcome: complete improvement with Immune suppression adjustment (raising steroid to 40mg and reducing mycophenolate mofetil (MMF) dose 30%) and mortality zero percent. Graft outcome in 1st 3-9 months post-transplant: 95.8% (23 patients) had good graft function (serum creatinine means SD (1.06±0.23) mg/dl). 4.16% (1 patient) had persistent serum creatinine 2.1mg/dl post-COVID-19 infection and did not need dialysis. Delayed graft function was found in 4 patients (16.6%). 2 patients (8.3%) suspected rejection that improved in less than 1 week without graft failure or needing dialysis.

Conclusion: Infection control measures against COVID-19 with Lower induction doses and immune suppression Adjustment are effective and associated with good renal graft and patients’ outcomes with mild to moderate COVID-19 infection.
Antibody Response to SARS-CoV-2 mRNA Vaccine in Kidney Transplant Recipients

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1Nephrology department, Hamad medical corporation, Doha, Qatar; 2Department of Laboratory Medicine and Pathology, Hamad medical corporation, Doha, Qatar; 3Weill Cornell Medical College in Qatar, Doha, Qatar

Introduction: Kidney transplant recipients are vulnerable to developing a severe form of COVID19 infection. Although severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccine has significantly improved incidence of COVID19, seroconversion rates in immunosuppressed patients post-vaccine are variable and unpredictable. We aimed to evaluate the rates of antibody response to SARS-CoV-2 mRNA vaccine, identify factors affecting immunogenicity, determine risk of infection and severity of COVID-19 infection among kidney transplant recipients.

Methods: We retrospectively reviewed 372 kidney transplant recipients who fulfilled the criteria. We categorized patients into three groups; previous infection, seronegative and seropositive patients. SARS-CoV-2 antibody response, risk factors associated with negative serology and patient’s outcomes were evaluated.

Results: There were 45 patients who had previous COVID-19 infection before measurement of anti SARS-Cov-2 antibodies; 20 patients before vaccination, 6 patients after the first dose of vaccine and 19 patients after the second dose. Of the remaining 327 patients, there were 250 patients (76%) who had seroconversion which were further categorized into low antibody (n=125) and high antibody groups. Factors associated with lower seroconversion included older age (p=0.06) and female gender (p=0.03), however Race, immunosuppression regimen, and trough levels were not significant. Analysis of variables associated with lower antibodies titer revealed older age (p= <0.0001), race (p= 0.02), history of diabetes (p= 0.04), and longer duration between antibodies titer measurement and 2nd dose of vaccine (p= 0.002) were significant. It was also found that seropositivity and previous COVID-19 Infection was associated with lower incidence of COVID-19 infection and Hospitalizations (Table 1, Figure 1).

Conclusion: Understanding the immunologic response to the SARS-CoV-2 vaccine in kidney transplant recipients is important to prevent life threatening infection. Identification of transplant recipients at risk of low vaccine response can be a guide to formulate personalized therapy.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Previous COVID-19 Infection (n=45)</th>
<th>No Previous Infection (n=327)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS CoV-2 antibodies titer</td>
<td>250 (250-250)</td>
<td>121 (25-250)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>COVID-19 Infection</td>
<td>6 (3.3)</td>
<td>28 (36)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>2 (4)</td>
<td>8 (13)</td>
<td>0.90</td>
</tr>
<tr>
<td>ICU admission</td>
<td>0</td>
<td>1 (1)</td>
<td>0.15</td>
</tr>
<tr>
<td>2nd dose Vaccine</td>
<td>31 (69)</td>
<td>184 (74)</td>
<td>0.65</td>
</tr>
<tr>
<td>Days between Antibodies titer and COVID-19 infection</td>
<td>165 (139-188)</td>
<td>179 (149-199)</td>
<td>0.55</td>
</tr>
<tr>
<td>Days between 2nd dose vaccine and COVID-19 infection</td>
<td>118 (96-119)</td>
<td>128 (100-133)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Time from antibody test to COVID-19 infection

P=0.007
P16.24

Drug-Related Problems Among Solid Organ Transplant Recipients Hospitalized for COVID-19: An Experience of A Referral Tertiary Center in Iran

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Backgrounds: Transplanted patients receiving immunosuppressive agents are at a higher risk of Coronavirus-disease-2019 (COVID-19), and their polypharmacy state makes the choice of treatment challenging. This study aimed to evaluate the drug-related problems (DRP) and clinical pharmacists’ interventions to manage transplanted patients and candidates for transplantation with COVID-19.

Methods: This cross-sectional study was conducted from March 2020 to April 2021 at the COVID-19 intensive care unit of Shiraz-organ-transplant center, Iran. Patients were admitted to the COVID-19 intensive care unit based on clinical presentations or positive polymerase chain reaction (PCR) tests. The clinical pharmacist daily reviewed all medications and physicians’ orders and evaluated DRPs regarding the pharmaceutical care network of Europe (PCNE) classification V8.01. The DRPs were informed to the treatment team, and the intervention acceptance or rejection was also recorded. Data were analyzed using SPSS V25.0. Descriptive statistics and logistic regression were performed to determine the proportion and determinants of drug-related problems, respectively.

Results: A clinical pharmacist reviewed 631 individuals with 11770 medication orders, and 639 DRPs were identified from 69% of participants with an average of 1.01±1 per patient. Problems related to treatment effectiveness were the most commonly reported DRPs followed by adverse drug reactions. A total of 982 interventions were provided at prescriber, patient, and drug levels, of which 801 were accepted, and 659 (82.27%) were fully implemented.

Conclusion: There have been considerable drug-related problems in managing transplanted patients with COVID-19. Those with polypharmacy, more than three comorbidities, and Hydroxychloroquine regimens are more likely to manifest DRPs.

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI) Univariate</th>
<th>P-value</th>
<th>OR (95% CI) Multivariate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.75 (0.44-1.23)</td>
<td>[0.88]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Age more than 50 years</td>
<td>2.75 (0.51-3.00)</td>
<td>[0.09]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>2.99 (1.20-2.76)</td>
<td>[0.039]</td>
<td>2.01 (1.88-2.91)</td>
<td>[0.039]</td>
</tr>
<tr>
<td>CNS*-based immunosuppressive regimen</td>
<td>1.70 (0.44-1.92)</td>
<td>[0.18]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Comorbid diseases more than 3</td>
<td>1.79 (1.20-3.29)</td>
<td>[0.001]</td>
<td>1.65 (1.50-2.77)</td>
<td>[0.023]</td>
</tr>
<tr>
<td>Transplantation</td>
<td>1.33 (1.19-3.98)</td>
<td>[0.001]</td>
<td>1.96 (1.14-2.85)</td>
<td>[0.046]</td>
</tr>
<tr>
<td>Remdesivir-based regimen</td>
<td>1.88 (0.33-1.91)</td>
<td>[0.68]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>High dose of corticosteroid based regimen</td>
<td>1.10 (0.60-1.32)</td>
<td>[0.10]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HCQ*-based regimen</td>
<td>3.91 (1.82-9.10)</td>
<td>[0.001]</td>
<td>2.81 (2.33-5.72)</td>
<td>[0.001]</td>
</tr>
<tr>
<td>Lopinavir-ritonavir based regimen</td>
<td>3.33 (0.66-2.90)</td>
<td>[0.07]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Length of ICU stay</td>
<td>1.27 (0.96-1.71)</td>
<td>[0.81]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>1.44 (0.19-1.70)</td>
<td>[0.29]</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Chloroquine, **Ivermectin, #Dexamethasone, $Lopinavir-ritonavir, &Remdesivir.
Immunoglobulin M (IgM) Delays Disease in K18-HACE2 Mice Infected With SARS-CoV-2

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1Surgery, University of Virginia, Charlottesville, VA, United States; 2Infectious Diseases, University of Virginia, Charlottesville, VA, United States; 3Center for Comparative Medicine, University of Virginia, Charlottesville, VA, United States

Introduction: IgM reverses new onset autoimmune type 1 diabetes and promotes graft survival by mitigating inflammation. It reprograms the immune system by inducing regulatory T cells, promoting the expression of micro-RNAs associated with the upregulation of regulatory immune cells, and repopulating dysregulated gut microbiome with beneficial bacteria. IgM also prevents HIV-1 viral entry into cells and protects mice from influenza virus infection and strep-pneumococcal infection. Therefore, the goal was to determine if IgM can delay or prevent disease in SARS-CoV-2 infected K18-hACE2 mice.

Method: 1) Vero E6 cells were used to test the effect of IgM in reducing the number of plaque-forming units (PFU). There were 4 groups: a) 25PFU WA-1 SARS-CoV-2 was combined with 20, 5 or 0.8 μg IgM in growth medium, and added to Vero E6 cells b) IgM was added to Vero E6 cells and incubated. The media was aspirated, and the cells were inoculated with 25PFU WA-1; c) Virus control - as above, but with no IgM; d) No virus or IgM. Following incubation with virus for 48 hours, virus replication was stopped and plates stained with Giemsa violet, dried, and photographed. 2) A COVID-19 Spike-ACE2 binding assay kit was used to determine if IgM (2ug, 4.5ug, 20ug, 45ug IgM) inhibited the interaction between the Spike-receptor binding domain (S-RBD) and Angiotensin I Converting Enzyme2 (ACE2) receptor. 3) K18-hACE2 mice were divided into 3 groups based on treatment regimen; Group 1: with IgM, No virus; 2: with Saline, with virus; 3: with IgM, with virus. 35ug IgM was injected intraperitoneal in a single dose, 2 days prior to infection. Mice were inoculated intranasally with 1250 pfu of HK SARS-CoV-2.

Results: 1) Exposure of 25PFU SARS-CoV-2 to IgM (at all concentrations) prior to incubation with Vero E6 cells, inhibited its replication in Vero E6 cells. When Vero E6 cells were incubated with IgM prior to infection, no plaques were seen in wells with 20ug and 5ug IgM but were observed in wells with 0.8ug IgM. Plaques were also observed in the Virus alone group, but none were seen in the “No IgM-No virus” group. 45ug IgM/100uls inhibited the binding of S-RBD to ACE2 by ~94-100%, 20ug IgM/100uls inhibited it by ~80%, and 2 or 4.5ug/100ul by ~70-75%. Control without IgM did not inhibit the S-RBD-ACE-2 binding. 3) Pretreatment with a single low dose IgM injection delayed weight loss and mortality.

Conclusion: IgM inhibits the replication of SARS-CoV-2 in Vero cells in vitro. It also inhibits the interaction between S-RBD that is present on the viral surface and the ACE2 receptor, by binding to S-RBD. A single low dose of IgM given prechallenge delayed disease in infected mice. The discovery that IgM interferes with the formation of the S-RBD-ACE2 complex, and that a single low dose can delay disease, indicates its translational potential as a vaccine/therapeutic to prevent or treat COVID-19.

We would like to acknowledge the “Focus to Cure Diabetes Foundation” which has enabled us to do this research.
Adenine A2A Receptor (A2AR) Agonists Improve Survival in K28-hACE2 Mice and Syrian Hamsters Following SARS-CoV-2 Infection

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Sanford Feldman3, Joel Linden4, Kenneth Brayman1
1Surgery, University of Virginia, Charlottesville, VA, United States; 2Infectious Diseases, University of Virginia, Charlottesville, VA, United States; 3Center for Comparative Medicine, University of Virginia, Charlottesville, VA, United States; 4Nephrology, University of Virginia, Charlottesville, VA, United States

**Introduction:** Apadenoson and Regadenoson protect animal and human lungs from ischemia-reperfusion or transplant injury. Our goal was to test their efficacy in attenuating hyper-inflammation and improving survival following SARS-CoV-2 infection of K18-hACE2 mice and Syrian hamsters.

**Method:** 6-8 weeks old K18-hACE2 mice were divided into Control group receiving vehicle; Test group 1 receiving drug (Apadenoson or Regadenoson) 15hrs prior challenge with SARS-CoV-2; and Test Group 2 (Drug-delay) receiving drug with a 5hr delay post-infection (n=18/group). 1250 PFU Hong Kong/VM20001061/2020 virus was delivered intranasally. Drug was delivered subcutaneously using ALZET pumps. 6 weeks old hamsters were divided into Control group receiving Vehicle and Virus (n=4) and 2 test groups (n=5/group) receiving Apadenoson+Virus and Regadenoson+Virus. Hamsters were inoculated intratracheally with 750PFU SARS-CoV-2 WA1 strain prior treatment. Bronchoalveolar lavage fluid and serum were collected along with lungs. Plethysmography was done on days 0, 2, 4 and 7.

**Results:** Apadenoson administered post-infection was efficacious in decreasing weight loss (P=0.002), improving clinical score (P=0.001), and increasing survival rate in K18-hACE2 mice, i.e. 85% survival at Day 7 for Test group 2 (P=0.0002) in Test group 1, and 12.5% for vehicle group. The levels of 13 cytokines/chemokines (IP-10, MIG, MCP-1, G-CSF, Eotaxin, MIP1β, VEGF, RANTES, INF-γ, IL-6, TNF-α, KC, LIF) in BALF were statistically different, with nine higher in virus-infected compared to uninfected controls (P<0.05). The levels of MIG, G-CSF, Eotaxin, MIP1β, VEGF, INF-γ, TNF-α, KC in Test group 2 were not significantly different from uninfected mice, except for IP-10 and MIG that were statistically higher. Notably, VEGF was lower in treated mice (P=0.011). Treated mice exhibited slower progression in weight loss without elevated cytokines and an increased chance of recovery. Increased Ang1-7 levels and decreased monocytes in BALF were also observed. Treated mice had undetectable viral titers, while all mice in Vehicle group had detectable titers. Treated mice also had lower viral burdens by IHC (P=0.0012). Viral burden on day 5 post-infection in treated mice negatively correlated with weight loss (P=0.0163). In Regadenoson studies, 42% of mice in Test group 1 survived infection compared to 6.25% in the vehicle or Test group 2. Viral titers in lungs of treated mice, and CD4+ and CD8+ T cells, eosinophils, and neutrophils in BALF were significantly decreased. In hamsters, significant improvement of pulmonary function parameters, RPEF and PenH, was seen with Apadenoson given post-infection. Apadenoson cleared the virus from BALF and maintained Ang1-7 levels. Both drugs decreased plasma IFN-γ levels.

**Conclusion:** Apadenoson attenuates inflammation, improves pulmonary function, decreases weight loss, and enhances survival rate following infection with SARS-CoV-2, supporting its use for treating COVID-19 patients. We would like to acknowledge the “Focus to Cure Diabetes Foundation” which has enabled us to do this research.
P16.28

COVID 19 Outcomes in Hospitalized Kidney and Kidney/Pancreas Transplant Recipients During Omicron Variant Wave

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A Total of 49 kidney and kidney pancreas transplant recipients were hospitalized with COVID 19 between December 2021 and February 2022. Mean age of patients was 51 years, 21 were females (42.8%) and 28 were males (57.1%). 24 patients (48.9%) were Hispanic, 23 patients (46.9%) were African American, 1 patient (2%) was Asian and 1 patient (2%) was Caucasian. 14 patients (8.1%) were within one year post transplantation. 28 of patients (57.1%) required oxygen therapy, 13 patients (26.5%) were admitted to intensive care unit and 10 patients died (20.4%). 22 patients were fully vaccinated against covid 19 (44.9%), 19 (38.7%) were partially vaccinated and 8 (16.3%) were unvaccinated. Among the unvaccinated group 5 (63%) required oxygen therapy, 2 (25%) patients admitted to the intensive care unit and subsequently died. Among the partially vaccinated group 12 (63%) required oxygen, 8 (42%) admitted to intensive care unit and 6 (32%) died. 2 of unvaccinated patients were admitted to ICU for hyperglycemia management rather than COVID 19 related symptoms. In fully vaccinated group 11 patients (50%) required oxygen therapy, 3 (14%) admitted to the ICU and 2 died (9%). one of the fully vaccinated patient was admitted to the ICU for hyperglycemia management. See Table 1.

Vaccination against COVID 19 may reduce severity and mortality rate in kidney and kidney/pancreas transplant recipients.

P16.29

Clinical Profile and Outcomes of COVID 19 Among Renal Transplant Recipients Across Three Waves of SARS CoV2 Infection: A Multicenter Study From South India

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Introduction: COVID19 has a devastating effect among renal transplant recipients. This study aimed to look at the clinical profile and outcomes of COVID 19 among renal transplant recipients across the three waves of SARS CoV2 infection in South India.

Methods: In this multicentre study conducted across three tertiary care hospitals in South India, we prospectively analysed all renal allograft recipients with microbiologically confirmed SARS CoV2 infection between June 2020 and February 2022. Transplant details, clinical features of severity, outcomes of COVID19 infection and risk factors associated with mortality were studied. The study was cleared by the Institutional Review Board of respective institutions and the guidelines of the Declaration of Helsinki were followed.

Results: We recruited 67 patients in this study with mean age of 44±11.5 years. Males were 67.2% of the cohort, 79.1% of patients were living donor transplant recipients, average transplant vintage was 6.6±5.5 years with a mean baseline creatinine of 1.47±0.81mg%. 37.3% of patients were diabetics. 56.7% of patients presented in the first wave, 22.4% in the second and 20.9% in the third wave. As per WHO clinical severity, 56.7% of patients had mild or asymptomatic infection, 17.9% had moderate infection and 25.4% had severe infection. The overall mortality was 17.9%. 35.8% of patients developed an AKI and 13.5% of patients required RRT. Severe infection was seen in 15.8% of infections in the first wave (44.9%), 19 (32.7%) were partially vaccinated and 8 (16.3%) were unvaccinated. Among the unvaccinated group 5 (63%) required oxygen therapy, 2 (25%) patients admitted to the intensive care unit and subsequently died. Among the partially vaccinated group 12 (63%) required oxygen, 8 (42%) admitted to intensive care unit and 6 (32%) died. 2 of unvaccinated patients were admitted to ICU for hyperglycemia management rather than COVID 19 related symptoms. In fully vaccinated group 11 patients (50%) required oxygen therapy, 3 (14%) admitted to the ICU and 2 died (9%). one of the fully vaccinated patient was admitted to the ICU for hyperglycemia management. See Table 1.

Vaccination against COVID 19 may reduce severity and mortality rate in kidney and kidney/pancreas transplant recipients.

n=49

<table>
<thead>
<tr>
<th>Mean Age in yr (median)</th>
<th>Not vaccinated (8)</th>
<th>Partially vaccinated (22)</th>
<th>Fully vaccinated (22)</th>
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<tbody>
<tr>
<td>Male 7 88% 9 47% 12 53%</td>
<td>48.5 (47)</td>
<td>50.6 (51)</td>
<td>53.5 (54)</td>
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<tr>
<td>Female 1 13% 10 53% 10 45%</td>
<td>55 54</td>
<td>52 53</td>
<td>53 54</td>
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<tr>
<td>Asian 0 0% 0 0% 1 5%</td>
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<td>45 45</td>
<td>45 45</td>
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<td>African american 6 75% 11 58% 6 27%</td>
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<td>52 53</td>
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<td>45 45</td>
<td>45 45</td>
<td>45 45</td>
</tr>
<tr>
<td>Hispanic 2 25% 8 42% 14 64%</td>
<td>55 54</td>
<td>52 53</td>
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<tr>
<td>Oxygen requirement 5 63% 12 63% 11 50%</td>
<td>55 54</td>
<td>52 53</td>
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<tr>
<td>ICU admission 2 25% 8 42% 3 14%</td>
<td>55 54</td>
<td>52 53</td>
<td>53 54</td>
</tr>
<tr>
<td>Mortality 2 25% 6 32% 2 9%</td>
<td>55 54</td>
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</table>

Conclusion: Renal transplant patients have higher mortality due to COVID 19 as compared to general population. Patients in the second wave of infection (presumably caused by Delta variant) had more severe disease, greater risk of AKI and higher mortality as compared to the first (Alpha variant) and third wave (Omicron variant) of SARS CoV2 infection.
Assessment of the Impact of the COVID -19 Pandemic on the Number of Brain Deaths, Family Donations, and Organs Used Between 2019-2020 in the Bursa Regional Coordination Center With the Most Donors in Turkey

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Introduction: The number of patients diagnosed with SARS-CoV2 worldwide in 2020 is 83,999,3791. According to the World Health Organization (WHO), 1,937,987 patients diagnosed with SARS-CoV2 died in 2020.2 In 2020, 2.3% of patients diagnosed with SARS-CoV2 died. The COVID-19 pandemic caused by SARS-CoV2 negatively impacts all sectors. One of the affected areas is organ supply and transplantation. The number of patients registered in the Transplant Dialysis Surveillance System (TDIS) waiting for solid organs in Turkey in 2020 is 23,923.3 The number of patients with family donations: 619, and the number of organs used: 2504. The number of brain deaths in 2019 was 1,391, the number of patients with family donations: 263, involved families donations. Of these, 1059 organs were used. This is 4.42% of the waiting patients.4 The inadequate supply of organs in our country Our study aimed to investigate the impact of the pandemic COVID-19 on the distribution of brain deaths reported in the regional coordination centers of Bursa, which has the highest number of brain deaths and family donations in Turkey by 2019-2020.

Materials and Methods: Using the data from the Transplantation Dialysis Monitoring System of the Ministry of Health - Decision Support Unit (TDIS-KDS), the distribution of brain death, family donation, and organs used data reported between 2019 and 2020 in Turkey was studied. This distribution retrospectively assessed the impact of the COVID-19 pandemic.

Results: According to the Transplant Dialysis Monitoring System (TDIS) data, there were 2,309 brain deaths in Turkey in 2019, patients with family donations: 619, and the number of organs used: 2504. The number of brain deaths in 2020: 1,391, the number of patients with family donations: 263, and the number of organs used: 1059.3 The number of brain deaths in 2019 Bursa Regional Coordination Center is 280, the number of patients with family donations: 117, the number of organs used: 222. The number of patients with brain death in 2020 is 208, the number of patients with family donations: 70 and the number of organs used: 104. In Turkey, the brain death rate in 2019 is 12.12%, the rate of patients family donations: 18.90% and the rate of organs used: 8.86%. In Turkey, the brain death rate in 2020 is 14.95%, the rate of patients family donations: 26.61%, and the rate of organs used: 9.82%. The COVID 19 pandemic has had a negative impact on organ donation rates and organ supply for solid organ transplants. However, with organ donation training in the provinces of the Bursa Regional Coordination Center, an increase in brain death rates, family donations, and organs used was observed in Bursa Regional Coordination Center in 2020.

Conclusion: The COVID19 pandemic has adversely affected patients awaiting solid organ transplants. The demand for cadaveric organ transplants has increased in Turkey. Patients without living donors are losing their lives. Social activities and legal incentives encouraging organ donation are increasing organ donation.
COVID-19 Clinical Outcomes, Coinfection and Secondary Infections in Solid Organ Transplant Recipients

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Introduction: The COVID-19 pandemic is still affecting the World. According to the Centers for Disease Control and Prevention, solid organ transplant (SOT) recipients are among those at high risk of serious illness from SARS-CoV-2. Because of the virus’s novelty, there is still a lack of information on topics such as how it behaves in immunocompromised hosts, how it affects immunosuppression, how it affects rejection, and whether it increases the incidence of opportunistic infections. In this study, we aimed to evaluate the clinical course of SOT recipients with COVID-19 over a one year follow-up period and to evaluate co-infections or secondary infections.

Method: Data from SOT patients diagnosed with COVID-19 has been retrieved retrospectively from the hospital information management system since March 2020. Demographic characteristics, examinations during hospitalization and admissions to outpatient clinics after illness were screened in detail.

Results: There were 53 SOT patients recorded. The median age was 49, the median time post-transplant was 11 years, thirty-four (71.7 %) were men. The kidney was the most frequently transplanted organ (75.5 %). Severe/critical COVID-19 was diagnosed within 11 (20.8%) patients. The most common symptoms were fever (49.1%) and cough (39.6%). Thirty-nine (73.6 %) of the patients were hospitalized. Among those 14 (26.4%) required mechanical ventilation, 8 (15%) required renal replacement therapy, and five (9.4%) died 7 days after diagnosis, 10 (18.8%) patients died 30 days after diagnosis. Co-infections occurred in 15 patients; there were six urinary tract infections, four bacteremia, two Cytomegalovirus (CMV), and one both with CMV and a urinary tract infection. During the follow-up, CMV and Aspergillosis were both detected in three patients, only CMV in one, only Aspergillosis in one, a healthcare-associated infection in one, and pancreatitis in one. All patients who developed CMV and/or aspergillosis had been given high dose steroid during their COVID-19 treatment. Two (3.7%) patients had acute rejection during this period.

Conclusion: The impact of immunosuppression on COVID-19 disease severity remains unclear. We believe that high-dose steroid therapy aids SOT patients who develop opportunistic infections such as CMV and aspergillosis. According to some studies, high-dose steroid therapy used to treat COVID-19 can cause opportunistic infections. In our study, we believe that the mortality rates were high due to our patients’ long post-transplantation period and, as a result, their chronic immunosuppression status. Wide-range studies are required to assess the long-term outcomes including allograft rejection, co-infections and secondary infections in SOT patients.
Introduction: Coronavirus Disease 2019 (COVID-19) pandemic had a significant impact on the field of kidney transplantation. Recipient was found to have high mortality associated with COVID-19 infection and also had vaccination-related problems. There was also a change in the habit of infection prevention activities in daily life. Clinicians were also more cautious before when screening donors and recipients, and had a practical and psychological effect on the timing of transplant surgery and the dosage of immunosuppressive agents. We conducted this study to understand whether there is a difference in new transplant outcome before and after COVID-19 pandemic when screening donors and recipients, and had a practical and psychological effect on the timing of transplant surgery and the dosage of immunosuppressive agents. We conducted this study to understand whether there is a difference in new transplant outcome before and after COVID-19 pandemic when screening donors and recipients, and had a practical and psychological effect on the timing of transplant surgery and the dosage of immunosuppressive agents.

Methods: From January 2018 to December 2021, patients who underwent kidney transplantation at Haeundae-paik Hospital were included in the study. We confirmed the living-donor or deceased donor transplantation, the presence or absence of rejection, hospitalization, the presence or absence of BK polyomavirus infection, and creatinine and cystatin C at 1 month, 3 months, and 12 months after transplantation.

Results: A total of 56 patients were included in the study. Prior to COVID-19 pandemic, 28 patients (male 20 and living donor transplants 10) underwent Kidney transplantation, and 28 patients (male 15 and living donor transplant 12) underwent surgery thereafter. The average age for each group was 54 ± 9.56 years and 53 ± 11.40 years. Rejection was 7 T-cell mediated rejection and 3 Antibody-mediated rejection in the group prior to COVID-19 pandemic, and 7 T-cell mediated rejection in the group after COVID-19 pandemic, with no statistically significant difference. There were 2 and 4 BK polyomavirus infections in each group. There were 7 hospitalizations per group within 1 year, and the average length of stay was 19.52 ± 32.68 days and 10.86 ± 89.34 days. Laboratory tests showed no statistically significant difference in creatinine and cystatin C levels at 1 month, 3 months, and 12 months.

Conclusion: There was no difference in the outcome of the kidney transplantation before and after COVID-19 pandemic when the treatment protocol and the transplant team in charge were the same.

Comparison of Kidney Transplant Outcomes Before and After Coronavirus Disease 2019 Pandemic: A Single-Institution Experience

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Native Kidney Infection Due to Non-tuberculous Mycobacteria Diagnosed by Molecular Multiplex Test in Renal Transplant: A Case Report

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Non-tuberculous mycobacteria (NTM) are acid-fast bacilli other than Mycobacterium tuberculosis (TBC). These organisms are ubiquitous in the environment and person-to-person transmission is considered an unlikely source. They can cause disease in both immunocompetent and immunosuppressed patients. Extrapulmonary NTM infections can occur due to breaches in the skin or soft tissues or due to several nosocomial factors. The diagnosis and differentiation of mycobacteria are carried out mainly through cultures and rapid molecular methods such as Real-Time Polymerase Chain Reaction (PCR), which in its multiplex format manages to rule out or confirm several molecular targets in a single reaction, speeding up thus the medical decision making.

Clinical case: 33-year-old male patient, related living donor kidney transplant, due to terminal chronic renal failure secondary to lupus nephritis. Immunosuppressive scheme: tacrolimus, prednisone, and mycophenolate. With a personal history of acute renal failure due to ureteral obstruction that required graft reimplantation to the native ureter. He was admitted for fever with chills for 9 days of evolution, lumbar pain in the right flank, and diarrhea. Inflammatory parameters were increased in blood and there were no isolates in cultures. He received empirical ceftriaxone and due to clinical improvement, he was discharged. The next day, he was re-admitted to the hospital due to the persistence of symptoms. Altered parameters in blood: Leukocytes 12.7 k/ul, erythrocyte sedimentation rate 93 mm/h, C-reactive protein 9.62 mg/dl, Creatinine 3.56 mg/dl and LDH 269U/L. Lumbar and abdominal CT scan: severe hydronephrosis in the right native kidney. A nephrostomy was performed. Blood culture: development of mycobacteria. PCR negative for mycobacteria in peripheral blood, but positive NTM in nephrostomy collection; also, discarding TBC by the same multiplex PCR. Treatment with ethambutol and clarithromycin was started. Radical nephrectomy of the right native kidney was performed, and histopathological analysis reported lesions consistent with uropyonephrosis/exacerbated chronic pyelonephritis. NTM infections in kidney transplants are uncommon, but when they do occur, the differentiation of NTM from TBC is of great clinical importance since it defines the isolation of patients in special rooms of health centers and the study of patient contacts. For that purpose, the implementation of molecular techniques has improved the diagnosis and differentiation of mycobacteria quickly and specifically concerning traditional culture. In our case, a multiplex PCR was used to detect targets of the genus Mycobacterium, the TBC complex, and the TBC species.

Although NTM infections in kidney transplant have been described, to our knowledge we describe the first case of infection caused by NTM in the native kidney of a renal transplant recipient, diagnosed by multiplex PCR.
P16.35

Pandemic Research in Organ Transplantation From India

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Introduction: In the beginning of pandemic, we emphasized on “the benefit to few versus risk to many” as a caution for continuing elective transplantation in resource limited nations like India.

Methods: Here we summarize all our research experience during the pandemic.

Results: We reported the comparative impact of pandemic from India in single center, national wide, and global observatory data on organ donation and transplantation. There was 50% decline in deceased donation transplantation in India contrasting with America, which was able to cope with the initial decline in transplants via a well-equipped deceased donation system. We contributed to National Organ and Tissue Transplant Organization (NOTTO), Transplant Specific Guidelines for COVID-19, NOTTO COVID-19 Vaccine Guidelines, NOTTO guidelines for Vaccine-induced thrombotic thrombocytopenia in organ donation, and consensus statement for kidney transplant recipient (KTR) and donor with a previous diagnosis of COVID-19. We first time reported that mortality rates in Southeast Asian KTR (n=250) with COVID-19 infection appear to be higher than those in non-immunosuppressed patients in our multicenter project. In nationwide data, we reported mortality in early kidney transplant recipients to be lower, and waitlisted patients to be higher which suggests, immunosuppression as per se is not an important factor in halting transplantation. We reported a different clinical spectrum of COVID-19 amongst KTR with similar mortality between the two waves. We were the first one to report safety of remdesivir (n=57) and convalescent plasma therapy (n=10) in organ transplant recipients. We reported the largest retrospective, multicentre, cohort study of KTR (n=31) from living donors who recovered from COVID-19. KTR (n=372) after recover from COVID-19, COVID-19-associated mucormycosis (CAM) with 4.4% incidence of CAM and 26.2% mortality, and with reoccurring SARS-CoV-2 infection(n=13), with 46% mortality. Our reports suggest that transplantation from COVID-19 donors may be feasible and safe, at least in short-term follow-up. In general, continuing a standard immunosuppression regimen may be reasonable, except in cases of inadvertent transplantation with active SARS-CoV-2. We reported COVID-19 vaccine safety with suboptimal efficacy in KTR and dialysis patients in a single-center experience. More research is needed to guide the optimal approach to a vaccination before and after transplantation.

Conclusion: We are continuing our research on vaccine efficacy, booster doses, and follow-up sequelae. Further policy-making and preparedness are required to safeguard the most vulnerable areas of the world to minimize the impact of any future pandemic on transplantation practices.

All contributing authors.

P16.36

Effectiveness of SARS-CoV 2 Vaccination in Kidney Transplant Patients in Chile

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Introduction: The humoral response to COVID-19 vaccines in transplant recipients has been reported to be lower than the obtained in the general population. For the Pfizer vaccine, antibody results are within 50-59% for those vaccinated or not, with the Sinovac vaccine, the degree of response to the Sinovac vaccine, the most used early in Chile, is unknown. Taking into account that the lethality of SARS-CoV-2 infection in transplanted patients was 6 times higher than the general population during the first wave of the pandemic (renal FUTAC data), we carried out this study with the aim of knowing the clinical effectiveness of the first two vaccines implemented in Chile in kidney transplant patients.

Methods: Prospective, observational, multicenter study. The FUTAC database was available with a periodic report from all transplant centers in the country with 98% coverage and information available from 3/27/2020 to 7/7/2021. The data of transplanted patients who were infected with SARS-CoV-2 were recorded comparing between those who had been fully vaccinated or not, with the Sinovac or Pfizer vaccine, evaluating the incidence of hospitalization and lethality. The group with complete vaccination was defined if the infection occurred 15 days after the second dose and the unvaccinated group corresponded to those without vaccination, with incomplete vaccination or in a period < 15 days after the second dose.

Results: Of a total of 424 cases, 16 were discarded due to incomplete data, analysing 408 patients, of which 530 (82%) suffered the infection without being effectively vaccinated and 72 (18%) who were fully vaccinated. Of the total patients fully vaccinated, 57% (40/70) received Sinovac vaccine and 43% (30/70) Pfizer. No differences were found between COVID-19 infection rates between 2020 and 2021. Of the fully vaccinated patients, 42/72 (58%) were hospitalized, and 14/72. (19%) died; in this group, there are 7 patients who are alive but seriously ill at the time of closing the registry. In the unvaccinated group, 53% (179/336) were hospitalized and 15% (50/336) died, without significant differences in hospitalization or fatality rates. No differences were found in hospitalization or fatality rates between those vaccinated with Pfizer or Sinovac.

Conclusions: The transplanted population, although fully vaccinated, maintains a high fatality rate, which is still 6 times higher than the general population. Although these data could be biased by the patients who did not consult, they were an input to decide a third dose of vaccination just applied to this highly vulnerable population, whose results are waiting to be evaluated. In Chile, the third booster dose was started in September 2021 and a 4th booster dose is currently being delivered starting in January 2022.

Marion Alarcon; Loreto Oliva; Silvana Morales.
Outcomes of COVID-19 Vaccination Among Kidney Transplant Recipients Admitted for COVID-19 at the National Kidney And Transplant Institute: A Retrospective Study

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Background: Kidney transplant recipients are immunocompromised hosts of COVID-19 with a higher risk of infection and severe disease due to underlying CKD and long-term immunosuppression, thus vaccination against COVID is strongly recommended. However, studies indicate that transplant recipients mount lower antibody responses following vaccination compared with healthy individuals. Due to limited information on the outcomes of COVID-19 vaccination on transplant recipients, this study will examine the efficacy of vaccination in preventing severe to critical COVID in this immunocompromised population.

Objective: To determine the outcomes of kidney transplant recipients admitted for COVID-19 at the National Kidney and Transplant Institute and the impact of COVID-19 vaccination status on their survival.

Methods and Materials: A retrospective study of 131 kidney transplant recipients admitted for COVID-19 from March 2020 to December 2021. Descriptive statistics were used to summarize the clinical characteristics and outcomes of the participants.

Results: The median age was 51 years old with a male gender distribution of 54.5%. Chronic glomerulonephritis was the most common primary renal disease. Diabetes, hypertension, and cardiovascular disease were the most common co-morbidities. Patients belonging to the critical COVID group were observed to have older kidney allografts with a median age of 120 months. Among 131 kidney transplant recipients, 24.8% were fully vaccinated and 74.2% were either unvaccinated or partially vaccinated. Of the 32 patients in the vaccinated group, 3 were vaccinated with Astra Zeneca, 5 received Janssen, 7 from Moderna, 10 from Pfizer, 1 received Sputnik and 12 received Coronavac (Sinovac). Among the vaccinated group, those who received Moderna and Pfizer vaccines were observed to have moderate COVID-19 disease progression only with 57.1% from the Moderna group and 40% from the Pfizer group. Among patients who progressed to critical COVID-19, it was observed that a significant number of them came from the Coronavac group.

The need for oxygenation was observed in 64% of patients, of which 65.5% were unvaccinated. Acute kidney injury was reported in 43.5% of the overall population, 63.2% of which were observed in the unvaccinated group. Of the 16% who had graft loss during COVID-19 admission, 57.1% from the Moderna group and 40% from the Pfizer group. Among patients who progressed to critical COVID-19, it was observed that a significant number of them came from the Coronavirus group.

Conclusion: Our experience shows that lack of COVID-19 vaccination among kidney transplant recipients demonstrates a higher rate of mortality associated with COVID-19.

Key words: COVID-19, renal transplantation, survival, Philippines.
Healthcare Resource Utilization in Transplant Recipients With Cytomegalovirus Infection Refractory to Prior Treatment With/Without Resistance Receiving Maribavir Versus Investigator-assigned Therapy: Exploratory Analysis of the Phase 3 SOLSTICE Trial

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Introduction: Increased healthcare resource utilization (HCRU) has been associated with cytomegalovirus (CMV) infection following transplantation, in particular in patients (pts) requiring >1 antiviral course. In the Phase 3 SOLSTICE study (NCT02931539), maribavir (MBV) was superior to investigator-assigned therapy (IAT; val/gra, foscar, cidofovir) for CMV clearance at Wk 8 and clearance plus symptom control Wk 8 maintained through Wk 16 in transplant recipients with refractory CMV infection with/without resistance (R/R). This exploratory analysis of SOLSTICE evaluated HCRU for the MBV and IAT arms.

Methods: Transplant recipients with CMV R/R to prior treatment (failure to achieve >1log decrease in CMV DNA after ≥14 days, with/without genotype resistance) were randomized 2:1 to MBV 400mg BID or IAT for 8 wks with 12 wks of follow-up. After ≥3 wks of treatment, pts in the IAT arm with pre-specified criteria could enter a MBV rescue arm (8 wks’ MBV treatment, 12 wks’ follow-up). Data on hospital admissions were collected at each study visit and analyzed by treatment during the treatment and follow-up phases. Analyses included the number of pts with ≥1 hospitalization and length of hospital stay (LOS). Hospitalization rates and LOS (per person/year) were estimated using negative binomial models adjusting for exposure time. Adjusted incidence rates (IR), 95% CIs, IR ratios (IRR) and percent reduction in IRRs were calculated. Supplementary analyses described hospitalizations and LOS for the rescue arm and individual IAT groups.

Results: In total, 352 pts were randomized (MBV: 235; IAT: 117), of whom 22 (18.8%) entered the MBV rescue arm. While on treatment, pts on MBV versus IAT had reductions of 34.8% in hospitalizations (p=0.021) and 53.8% in LOS (p=0.029; Table). Hospitalization rates were lower during the follow-up than treatment phase, with no differences between treatments in the follow-up (off-treatment) period (Table). The hospitalization rate in the IAT group pre-rescue with MBV (IR=6.98; 95% CI: 4.06, 12.03) was 2.54 times higher than on or after rescue with MBV (IR=2.75; 95% CI: 1.81, 4.18); increased LOS pre-rescue was also noted (IRR=2.25; 95% CI: 0.72, 7.01) but not statistically significant. In the IAT arm, foscar pts tended to have higher hospitalizations (5.5 admissions/person/year) and longer LOS (51.7 days/person/year) during the treatment phase compared with patients on val/gra or maribuvir (Figure).

Conclusion: Results from this analysis quantify the HCRU experience of pts requiring treatment for post-transplant CMV. Hospitalizations and LOS were lower for pts on MBV than IAT. Pts who received MBV rescue reported lower hospitalization rates on or after rescue than pre-rescue. Reducing hospitalizations is critical for alleviating disease burden to healthcare systems.

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Abstracts

P16.39

Immunogenicity of the Inactivated SARS-CoV-2 Vaccine (BBIBP-CorV; Sinopharm) And Short Term Clinical Outcomes in Vaccinated Solid Organ Transplant Recipients: A Prospective Cohort Study

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Introduction: Immunocompromised patients have lower seroconversion rate to Coronavirus disease 2019 (COVID-19) vaccination due to immune system dysfunction. So far, the majority of studies in this area are conducted on messenger ribonucleic acid (mRNA) based vaccines. The aim of this study is evaluation of humoral immune response and short term clinical outcomes in transplant patients vaccinated with SARS-CoV-2 Vaccine (BBIBP-CorV).

Methods: All patients older than 18 years old who had been transplanted more than six months prior to recruitment were included in this prospective cohort conducted in Shiraz transplant center as the largest transplant center in Asia from March to December, 2021. The patients received two doses of Sinopharm 4 weeks apart. The immunogenicity was evaluated through assessment of antibodies against the receptor-binding domain (RBD) of SARS-CoV-2 by enzyme-linked immunosorbent assay (ELISA) method 4 weeks after the first and second dose of vaccine. The patients were followed up weekly up to six months after the second dose and monthly up to six months after second dose and were evaluated for occurrence of vaccine adverse events, or getting COVID-19, hospitalization and laboratory parameters. The clinical and laboratory data of patients was recorded and analyzed by statistical tests.

Results: Totally, 921 transplant patients (665 kidney transplantation, 221 liver transplantation, 28 simultaneous pancreas kidney (SPK) and 7 heart transplant recipients). 115 (12.5%) and 239 (26%) patients had acceptable anti S-RBD IgG levels 4 weeks after the first and second dose, respectively. After omitting COVID19 cases with positive PCR test within 6 months before vaccination, 104 (12.6%) and 211 (25.5%) patients had acceptable anti S-RBD level 4 weeks after the first and second dose of vaccine. The patients were followed up weekly up to six months after the second dose monthly up to six months after second dose and were evaluated for occurrence of vaccine adverse events, or getting COVID-19, hospitalization and laboratory parameters. The clinical and laboratory data of patients was recorded and analyzed by statistical tests.

Conclusion: The results of our study showed that humoral response rate to Sinopharm vaccine was low in transplant patients. Short time from transplant was only effective factor on low seroconversion rate in transplant patients due to the high dose of immunosuppressive medications in this time frame. It is recommended that the third dose of vaccine, particularly from a different vaccine platform from the inactivated vaccine be administered in transplant patients.
Physicians' Opinions Regarding Low-Level Epstein-Barr Virus DNA Levels From PCR Testing

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Introduction: Epstein Barr virus (EBV) DNA measurement supports diagnosis and management of EBV-associated complications in transplant recipients. Laboratory-developed EBV DNA tests can be variable between laboratories and relatively insensitive. The availability of more sensitive, consistent and accurate tests, with results that are traceable to the WHO International Standard and are reported IU/mL of plasma, raises questions regarding the clinical importance of results in lower titer ranges that are newly detectable. Commercially available EBV DNA tests now exhibit sensitivity and even linearity near or below 100 IU/mL in plasma. With the advancement of more-sensitive diagnostics, the clinical significance of low-level EBV DNA test results should be considered, however, no clear clinical consensus is currently available to help interpret these results, and it is unclear what actions clinicians may take when presented with them. We undertook a survey of practicing adult and pediatric transplantation clinicians in order to characterize their likely therapeutic and diagnostic decisions in response to theoretical scenarios involving low-level EBV DNA test results.

Methods: Fifty-one clinicians who manage transplant recipients in the US, UK and Australia responded to a questionnaire presenting two hypothetical clinical scenarios involving low-level EBV DNA test results in adult and pediatric transplant patients. Scenario 1 included a detectable DNA level that was below the limit of quantitation. Scenario 2 involved low-level DNA results (150 vs. 400 IU/mL of plasma) from two different laboratories.

Results: Almost a quarter (24%) of clinicians would change treatment based on a single detectable EBV DNA result as presented in scenario 1 (Figure 1). Before changing treatment or ordering imaging studies in anticipation of possible core biopsy, the overwhelming majority would repeat EBV testing, mostly on a weekly basis. Most clinicians (59%) were likely to act based on the apparent increase in EBV DNA in scenario 2, with most intending to confirm the results through repeat testing to confirm the trend in viral load (Figure 2).

Conclusions: Adequate use and uptake of diagnostic testing in clinical medicine is often suboptimal leading to misinterpretation by clinicians and unnecessary diagnostic errors. Our findings reveal the impact that low-level EBV DNA plasma results may have on potential patient management approaches. In addition, the survey also showed marked differences in how clinicians would interpret and act on these results. This highlights that, in our theoretical clinical scenarios, there is no clear consensus regarding these potential and diverse interventions based on the different diagnostic and therapeutic approaches triggered by low EBV DNA plasma levels. These observed differences underline the need for more interpretive guidance to support the wider availability of more accurate, sensitive and standardized EBV DNA level monitoring assays.
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P16.41

Acute Kidney Rejection After Anti-sars-Cov-2 Virus-Vectored Vaccine – Case Report

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COVID-19 infection remains a threat to the health systems of many countries. A potential success in the fight against the COVID-19 pandemic is the vaccination of high-risk groups, including patients with end-stage kidney disease (ESKD) and after solid organ transplantation (SOT). Immunosuppression in kidney transplant recipients can also reduce the immunogenicity of SARS-CoV-2 vaccines (varied by vaccine platform), available data suggest that they are efficacious in approximately 50 – 70 %, compared to non-transplant situations.

In this paper, we present a newly developed acute humoral and cellular rejection with acute allograft failure and need of haemodialysis 14 days after administration of the adenovirus vectored SARS-CoV-2 vaccine (AstraZeneca; CHADOx1, AZD1222). This occurred in a patient who previously had an asymptomatic COVID-19 infection.

Case reports of acute allograft rejection after vaccination against SARS-CoV-2 can help stratify risk groups of patients who develop hyperimmune reactions. However, it is also possible that those with a previous mild primary COVID-19 infection may also develop acute allograft rejections upon COVID-19 re-infection.

Bioink Based on the dECM for 3D-Bioprinting of Bionic Pancreas - First Results of Animal

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Biomedical engineering is a fast developing discipline of science which combines the achievements of engineering and life sciences towards restoration and fabrication of complex physiological systems. Hence, the major challenge for biofabrication is mimicking natural extracellular matrix. Thus, bioink based on porcine, pancreatic ECM with semi-synthetic additives was develop. An extensive survey on obtained material was performed in both in vitro and in vivo tests. Petals of bioink with porcine islets was 3D printed and glucose stimulation tests was carried to verify the islets functionality. Insulin secretion assay showed that the bioink served appropriate conditions for islets which secreted significantly more insulin while compared to 2D islets culture. The cytotoxicity test of fabricated bioink on model L929 cell line was run and according to ISO 10993-5, the bioink appeared to be non-cytotoxic. Hence, in vivo experiments on murine model were performed. Animals with transplanted 3D constructs were examined for following parameters: AST, ALT, KC, IL-6 and TNF-α. Experiment took 12 months, and no disturbances of tested parameters were observed. Finally, mechanical properties of 3D printed constructs and their ultrastructure analysis were investigated. We conclude that newly developed bioink is appropriate for extrusion bioprinting and we proved to be non-cytotoxic. Furthermore, it constitutes a favorable conditions for the process of neovascularization which was noticed after 8 weeks after transplantation to animal model.
Towards Bionic Organs: Biocompatibility of Newly Developed Porcine dECM-Based Hydrogels

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Purpose: There is a growing interest in fabrication of bioinks which on one hand biocompatible and on the other hand possess mechanical properties which would allow to fabricate stable constructs capable to survive for a long time after transplantation. Although choosing appropriate material is essential for bioprinting, there is however, another, equally important issue extensively studied nowadays - inclusion of vasculature system within fabricated scaffolds.

Methods: In the following study we designed artificial channel bioprinted of ECM based so called “bioink A” to investigate if essential for neovascularization endothelial cells (HUVEC) and fibroblasts (aHDF) with proportions of 1:2 (8 mln/mL in total), would adhere to the material. Additionally, a media flow through such perfused channel was set to stimulate cell adhesion and proliferation. Fiber of bioink A which formed vault of a channel was printed either parallelly or perpendicularly to the direction of media flow. Two ways of seeding cells was tested. Channel was either printed with cell-laden so called “bioink B” or cells were delivered to the channel directly, with pipetting. In each seeding variant, a total of 4·105 cells per channel were used. After 2, 5, 8 or 24h of incubation, media flow was applied. After 8 days of experimental trial for each time variant, the channels were stored in formaldehyde and immunohistochemical staining was made to investigate the presence of cells on channel walls and vault.

Results: Cells adhered for both ways of fiber arrangement, however parallel bioprint with 5h of incubation and direct cell seeding resulted in better adhesion efficiency. After 5h of incubation, before flow was set, 2 1·105 cells stayed in channel with 75% viability. The quantity of cells did not decreased over time, until the end of experiment. Hematoxylin & Eosin staining showed that after 8 days cells were uniformly distributed across vault of a channel.

Conclusions: Our study clearly shows that cells which promote neovascularization adhere efficiently to pancreatic, ECM based bioink. It proves that bioink A of pancreatic origin can be used also for other than pancreatic cells type. Presented in this research bioink B can be used for other studies as vector for cell seeding.

Quadruple KO Porcine Adult Pancreatic Islet Induced Longterm Xenograft Survival in Diabetic Mice

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Introduction: Pancreatic islet transplantation has recently emerged as one of the most promising therapeutic approaches for improving glycemic control in Type 1 diabetes patients. However, there were some barriers like deficiency of islet supply due to shortage of pancreas and immune-mediated islet destruction after transplantation. Xenotransplantation using pig is one of the candidate species for clinical transplantation into patients with diabetes. But, some antigen are the obstacle to successful xenotransplantation. For these reasons, we isolated quadruple knockout (GGTA1/CMAH/Gb3s/B4GalNT2 knockout, QKO) islets and transplanted into STZ induced diabetic C57BL/6 and NOD-SCID mice. We identified transplanted QKO porcine islet efficiency in diabetic mice with/without immunosuppressive agent (anti-CD154, MR1).

Methods: Porcine pancreatic islets were isolated from 12 to 18 month old QKO pig using standard enzymatic digestion and purification. Recipients were injected STZ for diabetes induction (160 mg/kg, IP injection). Porcine islet were transplanted into the renal capsule of STZ induced diabetic C57BL/6 and NOD-SCID recipients (n=10 per group). To compare with QKO islet efficiency, we transplanted WT porcine islet into STZ induced diabetic C57BL/6 and NOD-SCID recipients with or without immunosuppressive agent. We monitored body weight, non-fasting blood glucose level and porcine insulin in serum. Intraperitoneal glucose tolerance test (IPGTT) in POD31 and 123.

Results: Transplantation of QKO and WT porcine islets under the kidney capsule into diabetic mice, hyperglycemia was reversed and became normoglycemia (BGL< 200mg/dL) at day 1. However, the WT porcine islet transplanted group became hyperglycemia within 7 days. On the other hands, QKO porcine islet transplanted group maintained normoglycemia up to 100 days without any immunosuppressive agent (p<0.05 ANOVA). Measured porcine insulin and c-peptide level in serum, normoglycemic mice detected was not increased. Transplantation of QKO islet in diabetic mice improved glucose profile and survival rate in STZ induced diabetic mice. Transplantation of transgenic pig islets could have a significant clinical impact on the treatment of type 1 diabetes. Key islet transplant studies in diabetic primates are currently underway.

Conclusion: In this study, we identified that xenotransplantation of QKO islets in diabetic mice improved glucose profile and survival rate in STZ induced diabetic mice. Transplantation of transgenic pig islets could have a significant clinical impact on the treatment of type 1 diabetes. Key islet transplant studies in diabetic primates are currently underway.
Feasibility and Safety of Intravenous Infusion of Autologous Umbilical Cord Blood for Newborns With Perinatal Hypoxic-Ischemic Encephalopathy: Argentina’s Experience

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Introduction: Perinatal hypoxic-ischemic encephalopathy (HIE) is a major cause of neonatal death and permanent neurological deficits. Stem cell therapy has recently been proposed as a novel therapy for HIE. Among the various sources, umbilical cord blood cells (UCBC) are readily available and can be exploited for autologous transplantations. Human umbilical cord blood (UCB) is a rich source of stem and progenitor cells. Furthermore, preclinical studies showed that the systemic administration of UCBC is beneficial for neonatal HIE.

Methods: The Ramón Sardá Maternity attends between 6,000 to 7,000 births per year. It is also a reference center for the care of high complexity pathologies of the newborns, including HIE. Garrahan Pediatric Hospital is a highly specialized medical pediatric public center. Among several services, it holds the National Public Cord Blood Bank (CBB). Both centers conducted a phase I clinical study to examine the feasibility and safety of intravenous infusion of autologous UCBC for newborns with HIE. When a baby was born with moderate/severe HIE, the UCB was collected, transported to the CBB, volume-reduced, divided into up to four doses, and transported back to the Maternity for infusion. This multicentre clinical study was approved by both Ramón Sardá’s Maternity and Garrahan Pediatric Hospital’s Institutional Review Boards and by INCUCAI Ethics Committee (Res N° 273/13).

Results: Between 2014 and 2019, 12 newborns were enrolled for the preclinical study. All babies received UCBC therapy together with therapeutic hypothermia. The processed UCBC were infused between 6–72 hours after the birth. Regarding feasibility, all patients received the doses within the first 24 hrs after birth, and 10/12 patients received the doses within the first 12 hrs. In terms of safety, there were no serious adverse events that might be related to cell therapy.

Conclusion: This pilot study shows that collection, preparation, and infusion of fresh autologous UCBC for use in infants with HIE is feasible and safe. A randomized double-blind study is needed to further explore whether it has beneficial effects.

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Comparison of Laboratory- And Clinical-Grade Reagents in Isolation and Cultivation of Human Amniotic Epithelial Cells

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Introduction: The human amniotic epithelial cell (hAEC) is a type of placental stem cell, which differentiates into all three germ layers. The hAECs have attracted attention as a new source of cell transplantation therapies and are considered to be suitable for clinical use from the following points. First, the hAECs are isolated from the delivered placenta and thus are readily available and easily procured without invasive procedures. Second, a sufficient number of hAECs can be obtained from a single human placenta. Third, hAECs do not possess tumorigenicity, unlike other pluripotent stem cells. Several preclinical studies using rodent models have shown the therapeutic potential of hAECs in the past decade. Now in the effort of clinical translation, preparation of the clinical protocol requires optimization of utilizing the clinical-grade reagents. In this study, we conducted a comparison experiment between laboratory-grade and clinical-grade reagents in isolation and cultivation of hAECs.

Methods: hAECs were isolated from the placentae of 3 patients who underwent scheduled Caesarean sections. Laboratory- and clinical-grade reagents were compared in cell isolation and cultivation for each case. Regarding hAECs isolation, total cell number per membrane amount (cell yield) and cell viability was evaluated. With several surface markers including CD49f and CD326 specific to hAECs, CD105 for stromal cells, and GlyA for hematopoietic cells, CD45 and CD31 for endothelial cells, purity of the hAEC was analyzed using flow cytometry. The rest of the isolated cells were cryopreserved in liquid nitrogen for three months. Thawing cells were cultured with laboratory- and clinical-grade media to evaluate cell viability and plating efficiency. Cell proliferation was examined using Cell Counting Kit-8 at the time points of 1, 3, and 5 days.

Results: The yield and viability of the isolated hAECs were equivalents between the laboratory- and the clinical-grade reagents. The purity of the cells was also sufficient (over 95% in both treatments), as no contamination of stromal cells or endothelial cells was detected. The cultured cells were well attached to plastic dishes, resulting in comparable viability and cell proliferation between the two groups.

Conclusion: The clinical-grade reagents were as suitable for hAECs isolation and cultivation as the laboratory-grade reagents. Using this protocol, we next prepared the clinical-grade hAEC products in our cell processing facility, which should be an important step for novel cell transplantation therapies.
Escape From Macrophage-Mediated Rejection by Human Surfactant Protein (SP)-A

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Introduction: Macrophage-mediated xenogeneic rejection is one of the important immunological obstructions that need to be overcome. Because macrophage is one of the main sources of proinflammatory cytokines and the fact that proinflammatory cytokines orchestrate a variety of inflammatory responses, the regulation of macrophages could result in solving the problem of xenogeneic rejection. We recently reported that membrane-type surfactant D (SP-D) on swine endothelial cells (SECs) suppresses macrophage-mediated rejection. Similar to SP-D, the carbohydrate recognition domain of surfactant protein-A (SP-A) induces inhibitory signals in effector cells. In this study, we examined the suppressive effect of SP-A on macrophage-mediated xenogeneic rejection.

Methods: Naïve SEC and SP-A-transfected SEC (SEC/SP-A) were co-cultured with THP-1 cells and cytotoxicity was evaluated. To investigate the effect on phagocytosis, human macrophages were co-cultured with SEC or SEC/SP-A, and the extent of phagocytosis and production of reactive oxygen species (ROS) were assessed by flow cytometry. The mRNA expression of inflammatory cytokines in macrophages was determined using RT-PCR. In addition, THP-1 cell with a luciferase reporter gene driven by an NF-kB response element (THP-1 Luc NF-kB) cells was used to verify their effects on the NF-kB transcription factors.

Results: The cytotoxicity of SEC/SP-A was significantly reduced compared to those of naïve SEC (40.7 vs 22.9%, p=0.025). The phagocytosis by macrophages against SEC was also significantly suppressed by SP-A on SEC (75.8 vs 33.0%, n=5, p=0.0010). Co-culture of human macrophages with SEC/SP-A decreased ROS production (%MFI: 99.9 vs 79.5, p=0.013). The mRNA expression of TNFα was reduced in macrophages (1.160 vs 0.009, p=0.0022), whereas that of IL-10 was increased (1.357 vs 10.20, p=0.0007). The balance between iNOS and Arg-1 was significantly suppressed by CL-SPA (1.002 vs 0.4792, p = 0.0027), indicating that CL-SPA on porcine cells inhibits the differentiation of peripheral blood monocytes into inflammatory M1 macrophages. The NF-kB transcription was reduced in THP-1 Luc NF-kB which was co-cultured with SEC/SP-A compared to that in THP-1 Luc NF-kB with SEC (RLU: 1160 vs 983.8, p=0.0258).

Conclusion: The ectopic expression of human SP-A in porcine cells represents an attractive method for suppressing macrophage-mediated cytotoxicity. To further investigate the effects of SP-A on xenogeneic innate immune response in more detail, in vivo studies should be performed in the future.

Comparison of Graft Survival Between Full Thickness And Lamellar Pig-To-Monkey Corneal Xenotransplantation From the Same Genetically Engineered Pig With Minimal Immunosuppression

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Introduction: Graft survival of full thickness corneal xenotransplantation with minimal immunosuppression is not well known. In comparison, lamella corneal xenotransplantation showed good results. We compare the graft survival between full thickness and lamella with the same genetically engineered pig.

Method: With the use of 3 transgenic pigs, six pig-to-monkey corneal transplantation was done. Two corneas from one pig transplanted to two monkeys with the fullthickness and lamella corneal xenotransplantations each. Transgenic type of donor pig is GTKO+CD46 in one and GTKO+CD46+TBM in two.

Results: Graft survivals of each xenotransplantation of GTKO+CD46 are 28 days and 28 days same. With the add of TBM, survival differences between lamella and fullthickness is 98 vs. 14 days and 119+(on-going) vs. 21 days. For failed graft, many inflammatory cells exist in grafts and no inflammatory cell in recipient’s stromal bed.

Conclusions: Lamella xenocorneal transplantation has the advantage of not having surgical complication such as retrocorneal membrane or anterior synechia seen in full thickness corneal xenotransplantation. In our study, graft survival of lamellar xenotransplantation is not well comparing with previous our experiments although superior survival period to fullthickness. Difference of graft survival based on the transpenic type is not definitive also. More cases and improvement of graft survival of lamella xenotransplantation will be needed to check the possibility of full thickness corneal xenotransplantation with the use of transgenic pig and minimal immunosuppression.
P17.09
CD27-Expressing Xenoantigen-Expanded Human Regulatory T Cells Are Efficient in Supressing Xenogeneic Immune Response

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Background: The clinical application of xenotransplantation often leads to T cell-mediated graft rejection. Immunosuppressive agents including polyclonal regulatory T cells (poly-Tregs) promote global immunosuppression, resulting in serious infection and malignancy in patients. Xenoantigen-expanded Tregs (xeno-Tregs) has become a promising immune therapy strategy that can protect xenografts with less side effects. In this study, we aimed to uncover a more efficient and stabler species of xeno-Tregs.

Methods: We enriched the CD27+ xeno-Tregs by cell sorting and evaluated their suppressive functions and stability in vitro via mixed lymphocyte reaction (MLR), RT-PCR, an inflammatory induction assay and western blotting. A humanized xenotransplanted mouse model was used to evaluate the function of CD27+ xeno-Tregs in vivo.

Results: Our results showed that CD27+ xeno-Tregs expressed higher levels of Foxp3, CTLA-4, and Helios and lower IL-17 than their CD27- counterparts. In addition, CD27+ xeno-Tregs showed significantly enhanced potency in suppressing the proliferation of xenoantigen-specific responder T cells at ratios of 1:4 and 1:16. Under inflammatory conditions, CD27+ xeno-Tregs displayed lower levels of IL-17 and IFN-gamma and less converted to IL17+ cells. Mice received porcine grafts showed normal tissue phenotype and less leukocyte infiltration after the injection of CD27+ xeno-Tregs. A humanized xenotransplanted mouse model was used to evaluate the function of CD27+ xeno-Tregs in vivo.

Conclusion: Taken together, these data indicated that CD27+ xeno-Tregs could suppress immune responses in a xenoantigen specific manner, effectively protecting xenografts from tissue damage.

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P17.10
Effect of Factor H on Complement Alternative Pathway Activation in Human Serum Remains on Porcine Cells Lacking N-Glycolyneuraminic Acid

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Background: Triple knockout (TKO) donor pigs lacking alpha-1,3-galactose (Gal), N-glycolyneuraminic acid (Neu5Gc), and Sd(a) expressions were developed to improve the clinical success of xenotransplantation. Neu5Gc, a sialic acid expressed on cell surfaces, recruits factor H to protect cells from attack by the complement system. Lack of Neu5Gc expression may cause unwanted complement activation, abrogating the potential benefit of gene-modified donor pigs. To investigate whether TKO porcine cells display increased susceptibility to complement activation in human serum, pathway-specific complement activation, apoptosis, and human platelet aggregation by porcine cells were compared between alpha-1,3-galactosyltransferase gene-knockout (GTKO) and TKO porcine cells.

Methods: Primary porcine peripheral blood mononuclear cells (pPBMCs) and endothelial cells (pECs) from GTKO and TKO pigs were used. Cells were incubated in human serum diluted in gelatin veronal buffer (GVB++) or Mg++-EGTA-GVB, and C3 deposition and apoptotic changes in these cells were measured by flow cytometry. C3 deposition levels were also measured after incubating these cells in 10% human serum supplemented with human factor H. Platelet aggregation in human platelet-rich plasma containing GTKO or TKO pECs was analyzed.

Results: The C3 deposition level in GTKO pPBMCs or pECs in GVB++ was significantly higher than that of TKO pPBMCs or pECs, respectively, but C3 deposition levels in Mg++-EGTA-GVB were comparable between them. The addition of factor H into the porcine cell suspension in 10% serum in Mg++-EGTA-GVB inhibited C3 deposition in a dose-dependent manner, and the extent of inhibition by factor H was similar between GTKO and TKO porcine cells. The percentage of late apoptotic cells in porcine cell suspension in GVB++ increased with the addition of human serum, of which the net increase was significantly less in TKO pPBMCs than in GTKO pPBMCs. Finally, the lag time of platelet aggregation in recalified human plasma was significantly prolonged in the presence of TKO pECs compared to that in the presence of GTKO pECs.

Conclusion: TKO genetic modification protects porcine cells from serum-induced complement activation and apoptotic changes, and delays calcification-induced human platelet aggregation. It does not hamper factor H recruitment on cell surfaces, allowing the suppression of alternative complement pathway activation.

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