Outcome Measures

RECIPIENT AND PANCREAS GRAFT SURVIVAL AFTER KIDNEY-PANCREAS TRANSPLANTATION IN AUSTRALIA AND NEW ZEALAND: A COHORT STUDY 1984–2014
WEBSTER Angela1,2, PENG Xi (Alex)2, KELLY Patrick2, and ANZIPTR On behalf of
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Background: We evaluated survival for kidney-pancreas recipients (SPK) in Australia and New Zealand.

Methods: Data 1984–2014 from the Australia and New Zealand Islet and Pancreas Transplant Registry were used to analyse time to pancreas failure (first of; pancreatectomy, insulin-dependence, with and without death) or death (all-cause), using Kaplan-Meier survival curves, censoring at last follow-up. We used Cox models (Hazard ratios HR, with 95%CI) to identify prognostic factors.

Results: We included 627 recipients, with 5,370 years of observation, 119 (19%) deaths and 214 (34%) pancreas failures. Patient survival was 97% at 1 year, 93% 5 years, 81% 10 years, 69% 15 years and 64% 20 years (figure). After adjusting for other differences, risk of dying decreased by 48% for people receiving SPK in 2010–2014 compared to 1989–1994 (HR0.52; P < 0.01). Recipient age increased risk of death 4% for every year older at transplantation (HR1.04; P = 0.04). There was no evidence of increased risk with any other factors (P > 0.05). Pancreas survival was 84% at 1 year, 76% 5 years, 64% 10 years, 56% 15 years and 50% 20 years. Pancreas failure decreased 40% between 1989–1994 and 2010–2014 (HR0.60; P < 0.02). After adjusting for other differences, risk of pancreas failure increased by 2% for every year of donor age (HR1.02; P = 0.03). There was some suggestion that longer time on RRT associated with higher risk of pancreas failure (P = 0.08).

Conclusion: There has been substantial improvement in patient survival and a substantial reduction in the risk of pancreas failure since SPK first began in ANZ.

OUTCOMES FOLLOWING TRANSFER OF PAEDIATRIC LIVER TRANSPLANT RECIPIENTS TO ADULT HEALTHCARE IN VICTORIA
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Background: Transition of children with chronic health issues to adult medical care is often associated with poor outcomes, stemming from noncompliance and psychosocial stressors.

This study aims to document health related outcomes within the Victorian paediatric liver transplant population, in the period following transition to adult care at Austin Health.

Methods: A retrospective search of the Victorian Liver Transplant Unit database and patient clinical records was performed to identify paediatric liver transplant recipients under the age of 18 as at 1st January 2000, who had been subsequently transitioned to Austin Health, and followed-up for a period of at least 12 months. Key outcome measures included medical nonadherence, chronic rejection, healthcare disengagement, evidence of ‘at risk’ behaviour, and active mental health issues. Nonadherence was defined as undetectable immunosuppressive serum drug levels or self-reported medication noncompliance.

Results: Of the 47 patients who met the inclusion criteria, 25 (53%) were adherent to medical therapy (Table 1). Rates of chronic rejection were 12% and 50% across the adherent and nonadherent groups respectively (P = 0.01), with a greater proportion of mental health issues noted amongst nonadherent patients (P = 0.02). Adherent patients were more likely to have higher rates of ongoing healthcare engagement, and miss fewer clinic appointments.

Conclusion: A significant portion of paediatric liver transplant recipients transitioned to adult follow up were nonadherent with
medical therapy, predisposing them to poorer health and transplant related outcomes. This suggests that our current model of transition needs to be improved.

**ASSOCIATION BETWEEN DELAYED GRAFT FUNCTION (DGF) AND GRAFT LOSS IN DONATION AFTER CARDIAC DEATH (DCD) DONOR KIDNEY TRANSPLANTS – A PAIRED KIDNEY ANALYSIS**

**Background:** Previous epidemiological studies have suggested that DGF is a risk factor for long-term graft loss in brain-dead donor kidney transplants but not DCD kidney transplants.

**Aim:** We aimed to determine the association between DGF and long-term overall and death-censored graft loss (DCGL) in DCD kidney transplants using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

**Methods:** Of the 201 paired DCD kidney transplant recipients identified between 1994–2012, 74 pairs were included because of differences in the presence of DGF (ie only 1 of the 2 recipients from the same donor experienced DGF, defined as requiring dialysis after transplantation). Associations between DGF and overall and DCGL were examined using adjusted Cox regression models.

**Results:** Of the 74 DCD donors, 50 (68%) were males with mean (SD) age of 45.2 (16.3) years. Recipients who had experienced DGF were of similar age and sensitization status compared to those who did not experience DGF. A greater proportion with DGF experienced DCGL (14% vs. 3%, p = 0.016). After adjusting for model covariates, DGF was associated with an increased risk of overall and DCGL at 5-years with adjusted hazard ratios of 2.82 (95%CI 0.91, 8.76) and 18.62 (95%CI 2.06, 168.29) respectively. Adjusted cumulative incidence curves for DCGL are shown in Figure 1.

**Conclusions:** DGF in DCD kidneys transplants is an independent risk factor for early graft loss after kidney transplantation.

**TABLE 1.** Demographic data and health outcomes

<table>
<thead>
<tr>
<th></th>
<th>Adherent</th>
<th>Non Adherent</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>25</td>
<td>22</td>
<td>0.01</td>
</tr>
<tr>
<td>Australian Born</td>
<td>24</td>
<td>21</td>
<td>1.00</td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>12</td>
<td>0.77</td>
</tr>
<tr>
<td>Median Age at Transplant</td>
<td>9.27</td>
<td>8.58</td>
<td>1.00</td>
</tr>
<tr>
<td>Median Age at Transfer</td>
<td>17.73</td>
<td>17.68</td>
<td>1.00</td>
</tr>
<tr>
<td>Chronic Rejection</td>
<td>3</td>
<td>11</td>
<td>0.01</td>
</tr>
<tr>
<td>Graft Loss</td>
<td>1</td>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>Healthcare Disengagement*</td>
<td>0</td>
<td>6</td>
<td>0.01</td>
</tr>
<tr>
<td>Missed &gt;3 Clinic Appointments</td>
<td>8</td>
<td>16</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>5</td>
<td>9</td>
<td>0.20</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2</td>
<td>4</td>
<td>0.39</td>
</tr>
<tr>
<td>Mental Health Issues</td>
<td>6</td>
<td>13</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*Consistent nonattendance at clinic for at least 12 months

**FIGURE 1.**
LONG-TERM GRAFT OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS WITH MEMBRANO-PROLIFERATIVE GLOMERULONEPHRITIS (MPGN)

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Aim: We aimed to determine the association between types of MPGN and long-term graft and patient outcomes using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

Methods: Primary live and deceased-donor kidney transplant recipients between 1990–2012 whose end-stage renal disease was attributed to glomerulonephritis were included. Associations between types of MPGN, acute rejection, all-cause mortality, overall and death-censored graft loss (DCGL) were examined using adjusted logistic and Cox regression models.

Results: Of 5532 kidney transplant recipients followed for a median (IQR) of 8.0 (3.7–13.1) years resulting in 48,692 person-years, 215 (3.9%) and 45 (0.8%) have type I and II MPGN respectively. Recipients with type I and II MPGN were older with mean age of 39.8 and 35.8 years compared to those with non-MPGN (43.7 years, P < 0.001). The incidence of overall (50%, 44% and 34% respectively, P < 0.001) and DCGL (42%, 38% and 22% respectively, P < 0.001) were higher in recipients with type I and II MPGN compared to non-MPGN. Compared to recipients with non-MPGN, the adjusted hazard ratios for overall graft loss for recipients with type I and II MPGN were 1.59 (95%CI 1.22, 2.08) and 1.63 (95%CI 0.99, 2.68) respectively; and were 2.10 (95%CI 1.57, 2.81) and 1.86 (95%CI 1.09, 3.17) for DCGL respectively. Graft loss attributed to recurrent MPGN in recipients with type I and II MPGN was 19% and 25%, with adjusted cumulative survival curves shown in Figure 1. There were no associations between MPGN, acute rejection and mortality.

Conclusions: Recipients with MPGN have poorer graft survivals with nearly one-quarter of recipients experiencing graft loss secondary to recurrent disease after a median of between 3–4 years.

FIGURE 1.

SEASONAL VARIATION IN KIDNEY TRANSPLANT OUTCOMES

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Background: Viral infection has been shown to be a risk factor for acute rejection after kidney transplantation. On epidemiological grounds, these results may support the hypothesis that winter months, which are associated with a higher risk of viral infections, are implicated in acute rejection. The aim of this study is to examine the relationship between seasonal changes and risk of acute rejection after kidney transplantation using ANZDATA registry.

Methods: Primary live and deceased donor kidney transplant recipients between 2004–2012 were included in this study. Association between seasons and acute rejection was examined using adjusted logistic and Cox regression analyses.

Results: Of 6108 kidney transplants performed, 1672 (27.4%), 1599 (26.2%), 1563 (25.6%) and 1274 (20.9%) were transplanted in the spring (September to November), autumn (March to May), winter (June to August) and summer (December to February) months respectively. A greater proportion of deceased donor transplants occurred in the summer compared to winter months (P = 0.037). For early rejection that occurred in the first 6 months after transplant and multiple rejections, transplants that occurred in the winter months were associated with higher risks compared to those that occurred in spring with adjusted odds ratios of 1.30 (95%CI 1.09, 1.56, P = 0.004) and 1.38 (95%CI 1.05, 1.82, P = 0.023) respectively. Compared to spring, the adjusted hazard ratio for any rejection of transplants that occurred during winter months were 1.20 (95%CI 1.04, 1.38, P = 0.011). There were no associations between seasons and risk of late rejection or types of rejection.

Conclusion: There appears to be a seasonal variation in the risk of acute rejection after kidney transplantation, independent of age, initial immunosuppression and sensitization status. It remains unknown whether this observation is an epiphenomenon or reflects the higher incidence of viral and other infections and future studies exploring the biological rationale of this association is required.

FIGURE 1.
REHABILITATION OUTCOMES FOLLOWING CARDIOPULMONARY TRANSPLANTATION AND INPATIENT REHABILITATION

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Background and Aim: For today’s transplant recipients, the median survival for heart transplant is 15 years, and for lung transplant 8 years (ANZCOTR data). This study aims to outline rehabilitation outcome data for this unique cohort of inpatients from 2004–2008, and to provide updated rehabilitation outcome data for the last 5 years (2009–2014).

Methods: From 2009–20014, there were 86 recipients of cardiopulmonary transplantation (32 heart and 54 lung) who completed inpatient rehabilitation programs at Sacred Heart Rehabilitation Services, St Vincent’s Hospital, Sydney. This represents 20% of the total number of transplant recipients treated under the Heart/Lung program at St Vincent’s Hospital. This retrospective audit examines rehabilitation outcome data for these patients. Trends regarding length of stay (LOS), complication rates and Functional Independence Measure (FIM) change will be presented showing variation in outcomes achieved.

Results: Results from the first cohort are discussed in Bowman 2013 (1). From 2009–2014, there were 32 patients with heart transplant, 37 rehabilitation admissions, an average LOS of 26 ± 26 days (mean ± standard deviation), admission FIM of 63 ± 18 and discharge FIM of 109 ± 20. There were 54 patients with lung transplant, 70 rehabilitation admissions, an average LOS of 22 ± 15 days, admission FIM of 81 ± 16 and discharge FIM of 98 ± 26.

Conclusions: Our inpatient program is uniquely designed to provide multidisciplinary rehabilitation to a population who require intense medical and surgical monitoring for rejection and side effects of anti-rejection drugs. Transplant recipients had similar LOS to the average LOS (23.4 days) at St Vincent’s Rehabilitation services, and represent 5-10% of the total inpatient rehabilitation admissions. Complexities in managing these patients include monitoring for complications of high levels of pharmacological immunosuppression, the management of chronotropic sequelae of transplantation.

References:

CIRCULATING SOLUBLE-KLOTHO LEVELS MODESTLY INCREASE AFTER RENAL TRANSPLANTATION

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1Department of Nephrology, Royal Melbourne Hospital, 2Department of Medicine, University of Melbourne, 3Department of Nephrology, Austin Hospital, Melbourne, 4Department of Nephrology, The Northern Hospital, Melbourne, VIC, 5Department of Endocrinology, St Vincent’s Hospital, Melbourne, 6Victorian Kidney Transplantation Collaborative, 7Department of Renal Medicine, Eastern Health, Box Hill Hospital, VIC, 8Department of Nephrology, St Vincent’s Hospital, Melbourne, 9School of Medicine, Deakin University

Background: Klotho, a co-receptor for FGF23, is predominantly expressed in kidney and reported to have anti-oxidant and anti-fibrotic properties. Soluble-Klotho (sKl), the circulating protein cleaved from membrane-bound Klotho, declines dramatically with kidney disease and is inversely associated with mortality. sKl has not been thoroughly evaluated prospectively after kidney transplantation.

Aim: To evaluate change in sKl over 12 months following kidney transplantation.

Methods: Incident kidney transplant recipients (KTRs) were recruited with blood sampled at 4 time-points; pretransplantation (baseline), 1-week (1w), 12-weeks (12w) and 52-weeks (52w) post transplantation. Samples were assayed for basic biochemistry and sKl (IBL, Japan). Within-subject comparisons were evaluated using repeat-measure ANOVA or Friedman’s analysis.

Results: Samples from 29 KTRs were available for final analysis. Median KTR age was 49 (35–55) years. Seventeen (59%) were male, 26 (90%) were living kidney allografts and 10 (34%) were preemptive. Table 1 summarises the change across the measured parameters. Compared with baseline, sKl exhibited an increase at 52w following initial decline at 1w (P < 0.005 and P < 0.01 respectively).

Conclusions: This prospective study demonstrated modest sKl increase post kidney transplantation despite excellent graft function achieved, suggesting factors beyond renal capacity influencing circulating sKl. Longer-term evaluation and investigation specifically addressing effects of immunosuppression on sKl are required to understand and modify the potential protective properties of sKl.

**Table 1.** Change in mineral metabolism parameters subsequent to kidney transplantation (n = 29)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>1-week</th>
<th>12-weeks</th>
<th>52-weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>sKlotho (pg/mL)</td>
<td>307 (279–460)</td>
<td>273 (246–343)</td>
<td>352 (286–417)</td>
<td>460 (311–629)</td>
</tr>
<tr>
<td>Serum phosphate (mg/dL)</td>
<td>1.78 ± 0.5</td>
<td>0.81 ± 0.29</td>
<td>0.88 ± 0.19</td>
<td>0.92 ± 0.17</td>
</tr>
<tr>
<td>Serum calcium (mg/dL)</td>
<td>2.40 ± 0.18</td>
<td>2.37 ± 0.20</td>
<td>2.46 ± 0.13</td>
<td>2.44 ± 0.13</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>36 ± 4</td>
<td>31 ± 3</td>
<td>38 ± 3</td>
<td>38 ± 4</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>638 (537–722)</td>
<td>113 (92–142)</td>
<td>112 (93–130)</td>
<td>111 (97–131)</td>
</tr>
<tr>
<td>eGFR ml/min/1.73m²</td>
<td>7.4 (6.5–8.7)</td>
<td>63.2 (46.5–87.4)</td>
<td>61.2 (51.7–71.9)</td>
<td>60.4 (50.5–71.8)</td>
</tr>
</tbody>
</table>

Data presented as Mean ± SD or Median (IQR). Friedman test with Dunn’s multiple comparisons performed for non-parametric values and repeat measures ANOVA performed for parametric values. *P < 0.005 compared with baseline. **P ≤ 0.01 compared with baseline. ***P < 0.005 compared with 7-day.
SCOPE AND HETEROGENEITY OF OUTCOMES REPORTED IN COCHRANE SYSTEMATIC REVIEWS OF KIDNEY TRANSPLANTATION

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Background: The heterogeneity and bias in selecting and reporting outcomes can limit the relevance and utility of systematic reviews (SRs) in informing shared decision-making. We aimed to assess the scope and consistency of outcomes reported in SRs for kidney transplant recipients.

Methods: The Cochrane Database of SRs was searched to November 2015 for published SRs of all interventions for kidney transplant recipients. All outcomes were extracted and clustered into domains, and the frequency of outcomes reported across all SRs was assessed.

Results: 30 SRs with 422 trials reported 1115 outcomes that clustered in 35 outcome domains. Only 5 outcome domains were reported in at least half of the SRs: mortality (29 SRs [97%]), graft function (25 [83%]), graft loss (24 [80%]), graft rejection (17 [57%]) and infection (15 [50%]). The next 3 most frequently reported outcomes were cancer (14 [47%]), cardiovascular diseases (13 [43%]) and lipids (10 [33%]). Patient-reported outcomes including mental health, health status, sleep, pain, physical function, were seldom reported (<20% of SRs). There was substantial variability in the tests, timing, and thresholds used to define and measure the outcomes.

Conclusions: Mortality and graft outcomes are frequently reported in Cochrane SRs of kidney transplantation, whereas other patient-centred outcomes including psychosocial status, mental and physical function are uncommon. These findings presumably reflect the outcomes reported in the corresponding trials. A standardised set of core outcomes based on the shared priorities of patients and health professionals in kidney transplantation may help maximise the value of SRs to inform clinical decision-making.

LONG-TERM GRAFT AND PATIENT OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS WITH AND WITHOUT TYPE II DIABETES MELLITUS (T2DM)

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Background: We aimed to determine the association between pre-transplant diabetes status and long-term outcomes in kidney transplant recipients using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

Methods: Primary live and deceased-donor kidney transplant recipients between 1994–2012 were included and associations between pretransplant diabetes status, all-cause mortality, overall and death-censored graft loss (DCGL) were examined using adjusted Cox regression models. Recipients with new-onset diabetes after transplantation are not identified by ANZDATA registry.

Results: Of 11,056 kidney transplant recipients followed for a median of 6.6 years resulting in 80,855 person-years, 985 (8.9%) had T2DM, of whom 655 (66.5%) had diabetic nephropathy recorded as cause of end-stage renal disease. Compared to recipients without diabetes, recipients with T2DM were associated with adjusted hazard ratios of 1.66 (95%CI 1.43, 1.93) for all-cause mortality; 1.38 (95%CI 1.15, 1.65) and 1.55 (95%CI 1.37, 1.76) for DCGL and overall graft loss respectively, with similar associations being observed across different eras of 1994–99, 2000–05 and 2006–12. Recipients with T2DM but without diabetic nephropathy had a lower risk of all-cause mortality with adjusted hazard ratio of 0.67 (95% CI 0.51, 0.88), particularly CVD mortality with adjusted hazard ratio of 0.41 (95%CI 0.25, 0.67) compared to T2DM recipients with established diabetic nephropathy.

Conclusions: Our findings suggest a continuing survival disadvantage in kidney transplant recipients with T2DM, particularly those with end-stage kidney disease attributed to diabetic nephropathy. This temporal trend is in contrast to improved survival for people with T2DM in the general population.
**REJECTION, GRAFT LOSS AND DEATH IN PAEDIATRIC AND ADOLESCENT KIDNEY TRANSPLANT RECIPIENTS**

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**Background:** We aimed to determine the association between acute rejection (AR) and long-term graft and patient outcomes of paediatric and adolescent kidney transplant recipients using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

**Methods:** Primary live and deceased-donor paediatric and adolescent kidney transplant recipients aged ≤21 years between 1997–2012 were included. Associations between AR, death-censored graft loss (DCGL) and all-cause mortality were examined using adjusted Cox regression models.

**Results:** Of 846 kidney transplant recipients followed for a median (IQR) of 7.2 (3.1–10.9) years resulting in 6104 person-years, 262 (31.0%) experienced AR. Recipients who had experienced rejection were significantly older compared to those who did not experience rejection (mean [SD] age 14.4 [5.8] vs. 12.6 [6.4], P < 0.001). Controlling for model covariates, any rejection was associated with DCGL with adjusted hazard ratio (HR) of 2.17 (95%CI 1.63, 2.89), with similar HRs for early rejection (occurring within first 90 days posttransplant; 1.49 [95%CI 1.06, 2.09]) and late rejection (occurring after 90 days; 2.10 [95%CI 1.52, 2.90]). Increasing number of episodes of AR was associated with an incremental risk of DCGL (referent: no rejection; 1 episode: adjusted HR 1.82 [95% CI 1.28, 2.58]; 2 episodes: adjusted HR 2.48 [95%CI 1.60, 3.84]; and ≥3 episodes: adjusted HR 2.97 [95% CI 1.86, 4.75]). Types of AR were associated with DCGL and all-cause mortality; with those experiencing vascular rejection have the poorest outcomes (adjusted cumulative survival curves below).

**Conclusions:** There is a strong association between rejection, particularly multiple rejections and vascular rejections and risk of DCGL and/or mortality in paediatric/adolescent kidney transplant recipients.
FIGURE 1.
LONG-TERM GRAFT OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS WITH PRESUMED GLOMERULONEPHRITIS (GN)

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Background: The transplant outcomes of end-stage renal disease (ESRD) patients with clinical diagnosis of presumed GN or uncertain diagnosis are unknown.

We aimed to determine the association between known and presumed diagnosis of GN and long-term graft outcomes using the Australia and New Zealand Dialysis and Transplant (ANZDATA) Registry.

Methods: Primary live and deceased-donor kidney transplant recipients between 1994-2012 whose end-stage renal disease was attributed to GN or “uncertain diagnosis” were included. GN was categorized into GN deemed at high risk of recurrence posttransplant (ie IgA nephropathy, membranoproliferative GN or primary focal segmental glomerulosclerosis – high-risk GN), other GN and presumed/advanced GN. Associations between GN types and death-censored graft loss (DCGL) were examined using adjusted Cox regression models.

Results: Of 6056 kidney transplant recipients followed for a median (IQR) of 7.9 (3.6-13.0) years resulting in 52,641 person-years, 2360 (39.0%), 1977 (32.6%), 1195 (19.7%) and 524 (8.7%) have a high-risk GN, other GN, presumed/advanced GN and uncertain diagnosis resulting in 52,641 person-years, respectively. A greater proportion of those with presumed/advanced GN and uncertain diagnosis cause of ESRD were indigenous patients and were older compared to the other GN groups (P < 0.001). Controlling for model covariates, the associations between GN categories and risk of DCGL and recurrent/de novo GN-related DCGL are shown in Table 1. The proportion of recipients who had experienced graft loss attributed to de novo/recurrent GN, including the types of recorded GN resulting in graft loss are shown in Table 1.

Conclusions: Recipients with presumed GN or uncertain cause of ESRD have a low risk of DCGL attributed to de novo/recurrent GN.

**TABLE 1.**

<table>
<thead>
<tr>
<th>GN categories</th>
<th>Adjusted hazard ratio (95%CI)</th>
<th>DCGL</th>
<th>De novo/recurrent GN-related DCGL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other GN</td>
<td>0.86 (0.73, 1.00)*</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>High-risk GN</td>
<td>0.93 (0.77, 1.11)</td>
<td>0.92 (0.64, 1.31)</td>
<td>0.34 (0.18, 0.65)*</td>
</tr>
<tr>
<td>Presumed/advanced GN</td>
<td>0.67 (0.50, 0.89)*</td>
<td>0.22 (0.07, 0.70)*</td>
<td>0.90 (0.71, 1.13)</td>
</tr>
<tr>
<td>Uncertain diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Incidence: GN-related graft loss.

**TABLE 1.**

<table>
<thead>
<tr>
<th>Delta eGFR</th>
<th>Adjusted hazard ratio (95%CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥15 ml/min/1.73 m² decline</td>
<td>1.36 (1.19, 1.56)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>-5 to &lt;15 ml/min/1.73 m² decline</td>
<td>1.12 (0.98, 1.28)</td>
<td>0.104</td>
</tr>
<tr>
<td>&lt;5 ml/min/1.73 m² decline</td>
<td>1.22 (0.91, 1.62)</td>
<td>0.362</td>
</tr>
<tr>
<td>to +5 ml/min/1.73 m² increase</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>+5 to &lt;15 ml/min/1.73 m² increase</td>
<td>1.05 (0.91, 1.21)</td>
<td>0.523</td>
</tr>
<tr>
<td>≥15 ml/min increase</td>
<td>2.99 (2.62, 3.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12-month eGFR</td>
<td>1.03 (0.89, 1.19)</td>
<td>0.680</td>
</tr>
<tr>
<td>&lt;30 ml/min/1.73 m²</td>
<td>1.24 (1.11, 1.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>30-&lt; 45 ml/min/1.73 m²</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>45-&lt; 60 ml/min/1.73 m²</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>≥60 ml/min/1.73 m²</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Results: Twelve-month eGFR was an effect modifier of delta eGFR between 6-12 months and overall graft loss (P-value for interaction 0.007). There was a parabolic association between delta eGFR and graft loss (deviation from linearity P < 0.001). Controlling for model covariates, there was an inverse association between delta eGFR and overall graft loss, which was more apparent in those with 12-month eGFR of at least 60 ml/min/1.73 m² (Table 1).

**TABLE 1.**

<table>
<thead>
<tr>
<th>Adjusted hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR &lt; 60 ml/min/1.73 m² (n = 2670)</td>
<td></td>
</tr>
<tr>
<td>Delta eGFR</td>
<td></td>
</tr>
<tr>
<td>≥-15 ml/min/1.73 m² decline</td>
<td>1.49 (1.01, 2.17)</td>
</tr>
<tr>
<td>-5 to &lt;15 ml/min/1.73 m² decline</td>
<td>1.51 (1.06, 2.13)</td>
</tr>
<tr>
<td>&lt;5 ml/min/1.73 m² decline</td>
<td>1.15 (0.91, 1.42)</td>
</tr>
<tr>
<td>to +5 ml/min/1.73 m² increase</td>
<td>1.00</td>
</tr>
<tr>
<td>≥5 to &lt;15 ml/min/1.73 m² increase</td>
<td>1.15 (0.94, 1.42)</td>
</tr>
<tr>
<td>≥15 ml/min/1.73 m² increase</td>
<td>1.22 (0.91, 1.62)</td>
</tr>
<tr>
<td>3-month eGFR</td>
<td>1.00</td>
</tr>
<tr>
<td>&lt;30 ml/min/1.73 m²</td>
<td>1.36 (1.01, 1.85)</td>
</tr>
<tr>
<td>30-&lt; 45 ml/min/1.73 m²</td>
<td>1.51 (1.06, 2.13)</td>
</tr>
<tr>
<td>45-&lt; 60 ml/min/1.73 m²</td>
<td>1.15 (0.91, 1.42)</td>
</tr>
<tr>
<td>≥60 ml/min/1.73 m²</td>
<td>1.22 (0.91, 1.62)</td>
</tr>
</tbody>
</table>

Data expressed as adjusted hazard ratios and 95% confidence intervals. Model adjusted for recipient age, gender, body mass index and donor age. eGFR – estimated glomerular filtration rate by MDRD equation.
Conclusion: Decline in eGFR between 6-12 months after transplantation, particularly those who have experienced at least a 15% decline, improved the risk stratification of graft loss independent of a single time-point eGFR. In recipients with 12-month eGFR of at least 60 ml/min/1.73 m², only delta eGFR and not single measurement of eGFR was associated with graft loss.

OUTCOMES OF LATE ANTIBODY MEDIATED REJECTION: SINGLE CENTRE RETROSPECTIVE STUDY

RUDERMAN Irene, MASTERNSON Rosemary, and HUGHES Peter
Renal & Transplantation Unit, Royal Melbourne Hospital

Background: Late antibody mediated rejection (AMR) is recognised as a major contributing cause to late allograft failure, with current therapies having little impact on graft outcomes.

Our aim was to identify predictors of outcome in a single centre transplant population with a diagnosis of late AMR and previously normal 3 month protocol biopsy.

Methods: We conducted a retrospective review of all renal transplant patients between January 2005 and December 2014. 106 patients were identified with late AMR using our local pathology database. 968 patients transplanted during the same period were used as control group.

Results: Median time to diagnosis of rejection was 58 months (range, 26–97) posttransplant. 33% of the cohort was ABO incompatible (ABOi). Preceding acute cellular rejection was found in 31% of patients. Class 2 de-novo donor specific antibodies (DSA) were present in 32%. When compared with the control group, the late AMR group had higher rates of ABOi and were younger.

Late AMR was associated with a 2 fold increased risk of graft loss compared to non-AMR controls. However history of ABOi, C4d positivity or de-novo DSA was not associated with worse graft outcomes. Predictably high chronicity scores on diagnostic biopsy were associated with worse prognosis.

Overall graft survival was poor in late AMR group, 58% of patients losing their graft during the study period with 50% graft survival at 40 months post late AMR diagnosis.

Conclusion: Late AMR continues to be a major posttransplant therapeutic challenge, with high rates of graft loss post diagnosis.
REVERSIBILITY OF FRAILTY IN HEART TRANSPLANT LISTED PATIENTS

JHA Sunita1,2, HANNU Malin1, NEWTON Phillip3, GORE KAREN1, WILHELM Kay4, HAYWARD Chris1, JABBOUR Andrew1, KOTLYAR Eugene1, KEOGH Anne1, DHITAL Kumud1, GRANGER Emily1, JANSZ Paul1, SPRATT Phillip1, MONTGOMERY Elyn1, HARKESS Michelle1, TUNNICLIFF Peta1, and MACDONALD Peter1

1Heart & Lung Transplant Unit, St Vincent's Hospital, Sydney, 2Faculty of Health, University of Technology Sydney, 3Faculty of Health, University of Technology, Sydney, 4Psychiatry, St Vincent’s Hospital, Sydney

Background: The aim of this study was to evaluate the reversibility of frailty in AHF patients undergoing bridge-to-transplant ventricular-assist-device (BTT-VAD) implantation and heart transplantation (HTx).

Methods: Since 2013, all AHF patients referred to our center were assessed for physical frailty (Fried phenotype, FP > 3/5 = frail) and a single-item measure of frailty (hand grip strength (HGS)) pre and post BTT-VAD/HTx. Results: 156 patients (109 M:47 F; age 53 ± 13 years, range 16–73; LVEF 27 ± 14%) were assessed for frailty. Prevalence was: frail 51 (33%) and not-frail 105 (67%). During listing, 31 patients underwent BTT-VAD implantation and 46 patients were transplanted. 8 frail pre-VAD and 5 frail pre-HTx patients were assessed at follow-up (avg. 17 days post-VAD and avg. 50 post-HTx). Frailty was significantly reversed in all patients who were classified as frail preintervention (Figure 1).

Conclusion: While frailty is predictive of increased mortality in patients referred for heart transplantation, surgical interventions have the potential to ameliorate cardiac-induced frailty.

FIGURE 1. Changes in frailty and hand-grip strength pre-post VAD/HTx.
THE VALUE OF SURVEILLANCE BIOPSIES AFTER PAEDIATRIC KIDNEY TRANSPLANTATION

ROSE Edward1,2, MACKIE Fiona2,1, and KENNEDY Sean1,2
1School of Women's & Children's Health, University of New South Wales, Sydney, 2Department of Nephrology, Sydney Children's Hospital

Background: To examine the benefit of surveillance biopsies performed 6 months after kidney transplantation in children.

Methods: A retrospective study of children transplanted at a single centre since 2005. Our protocol was to perform surveillance biopsies at 6 months. Excluded were highly sensitised recipients, ABO incompatible transplants and grafts with less than 12 months of follow-up.

Results: 35 kidney transplant recipients had a surveillance biopsy at a mean time of 187.9 ± 64.4 days after transplant. Recipients were followed for 1344 person-months (mean 38.4 months) with 97% graft survival. All recipients received induction therapy followed by triple immunosuppression including tacrolimus (n = 33) or cyclosporine (n = 2) prior to biopsy. Pathology was diagnosed on 24 (69%) of biopsies. Eight (23%) showed subclinical rejection (SCR, n = 1) or borderline SCR (n = 7); 6 of these were treated with pulse corticosteroids. Calcineurin inhibitor (CNI) toxicity &/or IF/TA was evident on 20 biopsies (57%), including 5 that had borderline SCR. BK nephropathy was diagnosed on 3 biopsies. 9 children had a reduction in CNI dose after biopsy and 7 were switched to sirolimus. The change in eGFR from 1 month after transplantation until the time of surveillance biopsy was not different between patients with biopsy-proven pathology and those with no pathology. Neither was there a difference in change eGFR from time of biopsy through to 3 months afterwards.

Conclusions: Pathology was evident on more than two thirds of 6 month surveillance biopsies. This information allowed adjustment of immunosuppression in the majority of patients without any evidence of harm.

DETERMINANTS OF TUBULAR MICROCALCIFICATION IN PROTOCOL BIOPSIES POST RENAL TRANSPLANTATION

JAW Juli1, LECAMWASAM Ashani2, COCHRANE-DAVIS Alex3, RICHARDS Avisha4, SUNDARARAJAN Vijaya5, HILL Prue6, and LANGHAM Robyn1,5
1Nephrology and Renal Transplant, St Vincent's Hospital, Melbourne, 2Department of Nephrology, Northern Health, 3Department of Medicine, Monash University, Melbourne, 4Department of Medicine, University of Dublin, Ireland, 5Department of Medicine, University of Melbourne, 6Department of Anatomical Pathology, St Vincent's Hospital, Melbourne

Background: Tubular microcalcification is a common histopathological feature, often recognised in early post transplant protocol biopsy. The presence of microcalcification is commonly thought to be a result of calcineuric inhibitor toxicity, though hyperparathyroidism and hypercalcaemia may also be predisposing risk factors. The clinical consequence of such finding is unclear, though it is assumed to be associated with inferior allograft function and survival. This study sought to identify clinical features associated with finding of tubular microcalcification in 3 month protocol biopsies.

Methods: A retrospective study was undertaken of routine 3-month protocol biopsies from 2006–2014, where microcalcification was described. Clinical history and serial biochemical data were collected (Table 1). Biochemical parameters were analysed at pretransplant and at 3, 6 and 12 months postransplant, along with immunosuppressant use and dose, as well as calcimimetic and calcium/phosphate supplementation.

Results: Tubular microcalcification was identified in 15 patients with mean creatinine of 121.3 ± 25.5 μmol/. CNI toxicity was detected in 1 patient, while metabolic acidosis was evidenced in 2 patients. PTH level was observed to be less than twice upper limit of normal. In 3 patients, tubular microcalcification was associated with allograft rejection. Of note, poorer graft outcome at 6 and 12 months was associated with pre transplant metabolic acidosis and use of calcium based phosphate binders (P < 0.05).

Conclusion: In this cohort, we observed no association between microcalcification and CNI toxicity or hyperparathyroidism. More studies are required to understand the genesis of tubular microcalcification in the acute transplant setting.
RECURRENT GLOMERULONEPHRITIS AND LONG-TERM GRAFT OUTCOMES AFTER KIDNEY TRANSPLANTATION

ALLEN Penelope¹, CRAIG Jonathan¹,², LIM Wai³,⁴, CHADBAN Steve²,⁵, ALLEN Richard²,⁵, and WONG Germaine¹,⁶
¹Centre for Kidney Research, The Children’s Hospital at Westmead, Sydney, ²School of Medicine, University of Sydney, ³School of Medicine & Pharmacology, University of Western Australia, Perth, ⁴Renal Unit, Sir Charles Gairdner Hospital, Perth, ⁵Royal Prince Alfred Hospital, Sydney, ⁶Renal Unit, Westmead Hospital, Sydney

Background: To determine the prevalence of recurrent glomerulonephritis and the risk of death-censored and overall graft loss in recipients with recurrent glomerulonephritis after kidney transplantation.

Methods: Primary live and deceased-donor kidney transplant recipients between 1997 and 2013 whose end-stage kidney disease (ESKD) was attributed to glomerulonephritis were included. We determined the association between the risk of overall and death-censored graft loss and recurrent disease using adjusted Cox proportional regression models.

Results: A total of 4,053 recipients were followed for a median follow-up time of 3.34 (IQR: 4.03) years. Glomerulonephritis was the commonest cause of ESKD (n = 1753, 43.3%), followed by congenital/genetic disease (n = 769, 19.0%) and diabetes (n = 431, 10.6%). The most common forms of glomerulonephritis were IgA disease (n = 650, 16.0%), focal segmental glomerulonephritis (n = 91, 2.25%) and mesangiocapillary glomerulonephritis (n = 60, 1.48%). A total of 87 recipients (out of 1753, 4.90%) experienced disease recurrence, with the median time to recurrence of 1.63 (IQR: 2.75) years. There were no significant differences in recipient characteristics with and without recurrence. Recipients with recurrent glomerulonephritis were more likely to lose their allograft than those without. The median time to graft loss for those with and without disease recurrence were 5.9 (IQR: 4.3) and 8.4 (IQR: 4.6) years, respectively. The adjusted HR for overall graft loss and death-censored graft loss were 1.41 [(95%CI: 1.12 – 1.75)] and 1.42 [(95%CI: 1.13 – 1.79)] (Figure 1).

Conclusions: Whilst there was a small risk of recurrent glomerulonephritis in the transplanted kidney, disease recurrence appeared to have significant impact on long-term graft survival even in the current era.

### TABLE 1.

<table>
<thead>
<tr>
<th>Baseline characteristic of patients (n = 15)</th>
<th>Mean ± SD (range)/n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>49.5 ± 12.2 (24–69)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13 (87)</td>
</tr>
<tr>
<td>Female</td>
<td>2 (13)</td>
</tr>
<tr>
<td><strong>Etiology of ESRD</strong></td>
<td></td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>6 (40)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Reflux nephropathy</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Renal cell carcinoma</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Primary oxalosis</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Medullary sponge kidney</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (13)</td>
</tr>
<tr>
<td><strong>Renal replacement therapy</strong></td>
<td></td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>6 (40)</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>6 (40)</td>
</tr>
<tr>
<td>No dialysis</td>
<td>3 (20)</td>
</tr>
<tr>
<td><strong>Donor age (years)</strong></td>
<td>41.9 ± 14.7 (20–71)</td>
</tr>
<tr>
<td><strong>Donor gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>7 (47)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (53)</td>
</tr>
<tr>
<td><strong>Type of transplantation</strong></td>
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</tr>
<tr>
<td>Cadaveric</td>
<td>11 (73)</td>
</tr>
<tr>
<td>Living donation</td>
<td>3 (20)</td>
</tr>
<tr>
<td>Kidney pancreas</td>
<td>1 (7)</td>
</tr>
<tr>
<td><strong>Graft function</strong></td>
<td></td>
</tr>
<tr>
<td>Delayed graft function</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Primary graft nonfunctioning (require dialysis)</td>
<td>3 (20)</td>
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<tr>
<td><strong>Immunosuppression</strong></td>
<td></td>
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<tr>
<td>Cyclosporine</td>
<td>4 (27)</td>
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<tr>
<td>Tacrolimus</td>
<td>9 (60)</td>
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<tr>
<td>Sirolimus</td>
<td>2 (13)</td>
</tr>
<tr>
<td><strong>Rejection</strong></td>
<td></td>
</tr>
<tr>
<td>T-cell mediated</td>
<td>2 (13)</td>
</tr>
<tr>
<td>Antibody mediated</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Calcineurin toxicity</td>
<td>1 (7)</td>
</tr>
<tr>
<td><strong>Graft survival at 12 years</strong></td>
<td>14 (93)</td>
</tr>
</tbody>
</table>
THE IMPACT OF DONOR-RECIPIENT AGE MISMATCH ON GRAFT AND PATIENT OUTCOMES AFTER DECEASED DONOR KIDNEY TRANSPLANTATION

CALISA Vaishnavi, CRAIG Jonathan, CHADBAN Steve, LIM Wai, HOWARD Kirsten, CHAPMAN Jeremy, MCDONALD Stephen, and WONG Germaine
Centre for Kidney Research, The Children's Hospital at Westmead, Sydney

Background: To determine the distribution of donor-recipient age differences and its influence on patient and graft outcomes after deceased donor kidney transplantation.


Results: A total of 3,025 recipients were followed for a median follow-up time of 2.9 years. The mean (SD: 13.7 years) age of the cohort was 49.5 years and 1,161 (38.4%) were female. The donor-recipient age differences were normally distributed [mean (SD) 3.8 +/- 20.0 years], confirming that it is not presently a criterion in assigning donor kidneys to recipients. A total of 212 (7.0%) recipients experienced allograft loss and 172 (5.7%) died with functioning grafts. The excess risk of mortality increased exponentially to 1.7 times (95%CI: 1.18, 2.35) when the donor was 40 years older than the recipient, but decreased asymptotically as the donor-recipient age differences fell below 0 (Figure 1). For every year increase in the donor-recipient age mismatch, the adjusted hazard ratios for overall graft loss and mortality were 1.016 (95%CI: 1.016, 1.023) and 1.013 (95%CI: 1.004, 1.022), respectively. Compared to those without donor-recipient age mismatches, older recipients who received kidneys from younger donors incur a significant survival advantage, with mortality risk decreased by up to 40% (95%CI: 15.2%, 57.5%), corresponding to a donor-recipient age difference of -40 years (Figure 1).

Conclusions: Reducing donor-recipient age mismatches may yield improved equity and utility in organ allocation.

FIGURE 1. Cumulative incidence of overall graft loss in recipients with and without recurrence.

THE IMPACT OF DONOR-RECIPIENT AGE MISMATCH ON GRAFT AND PATIENT OUTCOMES AFTER DECEASED DONOR KIDNEY TRANSPLANTATION

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Conclusions: Reducing donor-recipient age mismatches may yield improved equity and utility in organ allocation.

FIGURE 1. (on left) Relationship between adjusted hazard ratio for overall graft loss and donor-recipient age difference (on right) Relationship between adjusted hazard ratio for mortality and donor-recipient age difference.
THE ADDITION OF COGNITIVE IMPAIRMENT TO PHYSICAL FRAILITY IMPROVES SURVIVAL PREDICTION IN HEART-TRANSPLANT REFERRED PATIENTS

JHA Sunita1,2, HANNU Malin1, GORE Karen1, NEWTON Phillip3, HAYWARD Chris1, WILHELM Kay4, JABBOUR Andrew1, KOTLYAR Eugene1, KEOGH Anne1, DHITAL Kumud1, GRANGER Emily1, JANSZ Paul1, SPRATT Phillip1, MONTGOMERY Elyn1, HARKESS Michelle1, TUNNICLIFF Peta1, and MACDONALD Peter1

Background: The aim of this study was to identify whether the addition of cognitive impairment (CI) to the assessment of physical frailty (PF) better enhanced mortality prediction in heart-transplant referred patients.

Methods: Since 2013, all patients referred to our transplant center were consecutively assessed for physical frailty using an adapted

![Actuarial Survival](image)

![VAD/HTx free survival](image)

FIGURE 2. Actuarial and VAD/HTx-free kaplan-meier survival curves for physical and cognitive frailty.
version of Fried’s Phenotype. A patient was classified as frail if ≥3/5 domains were present. Assessment of cognitive impairment (Montreal Cognitive Assessment - MoCA) was also conducted at the time of frailty assessment. A patient was classified as ‘cognitively frail’ if ≥3/6 domains were present.

Results: 156 patients (109 M:47 F; age 53 ± 13 years, range 16–73; LVEF 27 ± 14%) underwent frailty assessment. Prevalence by physical frailty was: Frail 51 (33%) and 105 (67%) nonfrail. Prevalence by cognitive frailty was: Frail 62 (40%) and 94 (60%) nonfrail. Frailty, either physical or cognitive, was associated with lower BMI, NYHA class IV, hypoalbuminaemia and anaemia (P < 0.01). Cognitive frailty was additionally associated with increased right arterial pressure and lower cardiac index (P < 0.05). Actuarial survival curves are shown in figure 1 for physical (a) and cognitive (b) frailty. Survival adjusted for bridge-to-transplant ventricular assist device (BTT-VAD) and heart transplant (HTx) are also shown in figure 1 (c)/(d).

Conclusion: Cognitive frailty was highly prevalent and the addition of CI to PF, provided a better predictor of early mortality in transplant referred patients.

AGREEMENT BETWEEN NUMBER OF DONOR/RECIPIENT EPLET MISMATCHES CALCULATED USING 2-DIGIT SEROLOGICAL VERSUS 4-DIGIT MOLECULAR HUMAN LEUKOCYTE ANTIGEN (HLA)-TYPING

FIDLER Samantha1, WONG Germaine2, LEWIS Joshua3, and LIM Wai4

1Department of Clinical Immunology, Fiona Stanley Hospital, 2Westmead Millennium Institute, Westmead Hospital, Sydney, 3University of Sydney, 4Sir Charles Gairdner Hospital, Perth

Background: We aimed to assess the agreement of the number of eplet mismatches at the HLA-A, −B, −C, −DQ and -DR loci determined by 2-digit serological and 4-digit molecular typing.

Methods: We included patients who received live or deceased-donor kidney transplants between 2003 and 2007. Donor and recipient serological typing was determined using complement-dependent cytotoxicity, and molecular 4-digit typing determined using sequence based typing (Sanger). The number of eplet mismatches was calculated by converting the 2 and 4-digit HLA-typing using HLAMatchmaker. Correlation and agreement of HLA-A, −B, −C, −DP and -DR mismatches between the 2 methods was analysed using Spearman rank correlation and Bland Altman plots respectively. HLA-DP can only be determined using 4-digit typing and therefore not included in this study.

Results: Of 264 kidney transplant recipients, 86 (33%) were females. The correlation between class I (HLA-A, −B, −C) and class II (HLA-DQ, −DR) between 2 and 4-digit converted eplet mismatches were 0.966 and 0.931 respectively. Bland-Altman’s limits of agreement between class I, class II and combined class I and II eplet mismatches using 2 and 4-digit typing is shown below (figure 1). The number of class I and II eplet mismatches determined by 4-digit conversion exceeded that of 2-digit conversion in 37% of recipients, with 10% exceeding 7 eplet mismatches. One hundred and sixteen (44%) recipients had identical number of class I and II eplet mismatches as determined by 2 and 4-digit typing. Of the 21 “outliers” for both class I and II eplet mismatches, 5 (24%) of patients were females and 8 (38%) of either patients or donors were nonCaucasians. A further 4 (19%) had unusual (nonCaucasians) HLA alleles.

Conclusions: It appears that there is good correlation and agreement between 2 and 4 digit typing for total eplet mismatches at the HLA-A, −B, −C, −DQ and -DR loci. Future research should focus on exploring the clinical significance of total eplet mismatches determined by the 2 different methods.
Background: Chronic lung allograft dysfunction (CLAD) remains 1 of the major barriers for long-term survival following lung transplantation. We previously found in cystic fibrosis lung transplant recipients that re-colonization of the allograft (concordance) with Pseudomonas was not associated with CLAD, while de novo acquisition (discordance) was associated with CLAD, however the mechanism(s) remain unknown. In this study we investigated the possibility that a concordant microbiome might induce tolerogenic innate immune machinery, favouring graft survival.

Methods: This retrospective, cross-sectional study was performed on stored bronchoalveolar lavage (BAL) samples. Pre and posttransplant bacterial cultures were used to classify patients into concordant or discordant microbiome groups. BAL cellularity was determined. Markers of innate immune activation (mannose-binding lectin (MBL), IL-1β, IL-6, IL-8, IL-10, TNFα, TGF-β), M1 (TNFα, IL-1β, IL-6, NOS, ICAM-1) and M2 (IL-10, arginase, TGF-β, CD36, macrophage scavenger receptor 1 (MSR1)) macrophage subtypes were assayed.

Results: There was no association between any patient demographic (time posttransplant, age, pretransplant diagnosis) and any outcome measure. There was no association between any innate immune marker or BAL cellularity and microbial concordance (p > 0.05). A concordant microbiome was associated with increased levels of ICAM-1 (Odds ratio (95% CI), 1.81 (1.12–2.93), p = 0.016), TNFα (2.41 (1.33–4.35), p = 0.004), and NOS2 (1.25 (1.02–1.53), p = 0.036), all markers associated with an M1 macrophage phenotype, and IL-10 (1.81 (1.16–2.83), p = 0.009), an M2 macrophage associated marker.

Conclusions: Microbial concordance was associated with a skew towards an M1 macrophage pattern. These observations are consistent with the idea that macrophage polarisation, induced by the microbiome, may lead to skewing away from the profibrotic M2 phenotype, hence limiting immune injury, airway fibrosis and CLAD development.

### TABLE 1.

<table>
<thead>
<tr>
<th>Consistency</th>
<th>Absolute agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Digit</td>
<td>4 Digit (95% CI)</td>
</tr>
<tr>
<td>HLA-A</td>
<td>0.995 (0.994-0.996)</td>
</tr>
<tr>
<td>HLA-B</td>
<td>0.983 (0.978-0.987)</td>
</tr>
<tr>
<td>HLA-C</td>
<td>0.875 (0.843-0.900)</td>
</tr>
<tr>
<td>Class I</td>
<td>0.969 (0.960-0.975)</td>
</tr>
<tr>
<td>HLA-DR</td>
<td>0.987 (0.984-0.990)</td>
</tr>
<tr>
<td>HLA-DQ</td>
<td>0.810 (0.764-0.848)</td>
</tr>
<tr>
<td>Class II†</td>
<td>0.935 (0.918-0.949)</td>
</tr>
</tbody>
</table>

*Two-way fixed intraclass correlation coefficients. †Excluding HLA-DP.
ROLE OF MHC CLASS I MOLECULES AND CO-STIMULATORY MOLECULES IN RODENT MHC MISMATCH SKIN TRANSPLANT MODELS
LEON G Mario1, PAUL Moumita2, MOUAWADH Mamdoh2, CUNNINGHAM Eithne2, TAY Szun Szun2, WANG Chuanmin2, BERTOLINO Patrick2, BOWEN David2, BISHOP Alex2, ALEXANDER Ian2, and SHARLAND Alexandra2
1School of Medicine, University of Sydney, 2Department of Surgery, University of Sydney

Background: Expression of allogeneic MHC class I by recipient hepatocytes following inoculation with a liver specific AAV vector results in tolerance to subsequent skin grafts expressing the same mismatched MHC allele. Tolerance may result from direct recognition of intact allogeneic MHC on hepatocyte surface or from indirect recognition of processed peptides. D227K mutant class I molecules cannot be directly recognized by majority of alloreactive T-cells. Hepatocytes are nonprofessional antigen presenting cells and lack expression of co-stimulatory molecules. It is postulated that CD86 expression may negate their ability to induce tolerance in alloreactive CD8+ T-cells.

Methods: C57BL/6 mice were inoculated with AAV-Kd doses ranging from 5x10^9 to 5x10^11 vgc or AAV-D227K-Kd at 5x10^11 vgc. Some mice also received AAV-CD86. All mice then received Kd skin grafts. Skin graft survival, liver inflammation and Kd expression were monitored.

Results: There was dose-dependent prolongation of survival of Kd skin grafts, culminating in indefinite survival for all grafts at 5x10^11 vgc. Inoculation with AAV-D227Kd improved median graft survival from 15 to 29 days. Co-expressing CD86 abrogates tolerance induction (MST 20 days) and was accompanied by significant hepatic inflammation and CD8+ infiltration. By the time of graft rejection, Kd expression had been lost in most hepatocytes, in contrast to tolerance where it persists long term.

Conclusions: Dose-dependent prolongation of Kd-mismatched skin graft survival was achieved by administration of AAV-Kd in C57BL/6 mice. Tolerance was not induced in the absence of direct MHC class I recognition and was abrogated when CD86 was co-expressed on hepatocytes.

STIMULATION WITH ANTIGEN AND CYTOKINES INDUCE EXPRESSION IRF4 IN NAÏVE CD4+CD25+ T REGULATORY CELLS
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Background: We have previously shown that enriched naïve CD4+CD25−Foxp3+ Treg cultured for 3-4 day with alloantigen and IL-2 generate antigen-specific Treg. 10-30% are induced to express CD8 as well as CD4, and these are thought to be the cells stimulated by their TCR recognizing alloantigen.

We examined if the transcription factor IRF4, which is induced by antigen binding to TCR, was increased in these antigen specific Treg.

Method: Naive CD4+CD8−Foxp3+ Treg were prepared from normal DA rats, and cultured for 4 days with PVG alloantigen and IL-2. Cultured cells separated to CD8+ and CD8− were analyzed by FACS, RT-PCR, and for capacity to suppress in vivo and in MLC.

Results: These cultures induce expression of IFN-γR, and the cells have enhanced capacity to suppress both proliferation in MLC at 1:32-1:64 and graft rejection in vivo to induce tolerance. The CD4+CD8−Foxp3+ subpopulation suppress MLC in an Ag-specific manner at ratios of 1:1056, while CD4+CD8− cells showed no increase in potency. These CD8+ cells are essential to their capacity to suppress rejection and induce tolerance. This suggests CD8+ cells recognized alloantigen.

IRF4 was not detected in naïve CD4+CD8−Foxp3+ Treg, yet was induced by culture; IRF4 expression was much greater in the CD4+CD8− cells than the CD4+CD8−. Similar induction of IRF4 has been observed in naïve Treg cultured with antigen and IL-4.

Conclusion: Our data are consistent with the hypothesis that the CD4+CD8− cells are the activated Ag-specific Ts1 cells, and induction of IRF4 may be a marker of antigen activated Treg.
TARGETED MODIFICATION OF DC PHENOTYPE AND FUNCTION WITH POROUS SILICON NANOPARTICLES

STEAD Sebastian 1, 2, McINNIES Steven 3, KIRETA Svetlana 2, ROSE Peter 3, ROJAS-CANALES Darling 2, JESUDASON Shilpa 2, GREY Shane 2, CARROLL Robert 2, VOELCKER Nico 3, and COATES Toby 2, 1

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Background: Dendritic cells (DC) are the most potent antigen-presenting cell and are fundamental in the establishment of transplant tolerance. Targeting DC via the DC-SIGN receptor is a potential target for cell specific therapy. Porous silicon nanoparticles (pSiNP) loaded with immunosuppressant rapamycin (RAPA-pSiNP) provides a unique platform to target and modify DC in vivo. The aim of this study was to conjugate monoclonal antibody anti-DC-SIGN on to the surface of RAPA-pSiNP and determine the effects on targeted DC phenotype and stimulatory capacity in vitro.

Methods: Fluorescein isothiocyanate (FITC)-labelled pSiNP conjugated to either anti-DC-SIGN or isotype control were cultured with whole blood samples in vitro to assess specific targeting of DC. Uptake was determined via flow cytometry and transmission electron microscopy. Rapamycin loading of pSiNP was confirmed with ultraviolet visualisation and inferred spectrometry. DC were co-cultured with rapamycin loaded pSiNP for 2 days (± LPS), irradiated and co-cultured with CFSE stained allogeneic T-cells.

Results: Anti-DC-SIGN pSiNP favourably targeted and were phagocytised by myeloid DC in whole blood samples in a time and dose dependent manner. Myeloid DC were 42% positive for Anti-DC-SIGN functionalised NP compared to only 10% for isotype control and 5% for unfunctionalised NP. DC preconditioning with RAPA-pSiNP results in a maturation resistant phenotype and significantly suppresses allogeneic T-cell proliferation by 28.6 ± 1.9% (p < 0.0001).

Conclusions: RAPA-pSiNP conjugated to anti-DC-SIGN actively targets and modifies DC function and may serve as a novel therapy to target DC in vivo.

EXPRESSION OF 3 ALLOGENEIC MHC CLASS I IN RECIPIENT LIVER SIGNIFICANTLY PROLONGS SURVIVAL OF FULLY-ALLOGENEIC VASCULARISED CARDIAC ALLOGRAFTS

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Background: In previous studies, AAV-mediated gene transfer of a single mismatched donor MHC class I molecule (Kd or Kb) to C57BL/6 or B10.BR recipient liver respectively induced tolerance to skin grafts expressing the same mismatched MHC molecule. However, such survival is not extended to fully mismatched skin or heart grafts. Tolerance induction may require expression of all mismatched MHC molecules (3 class I and 2 class II). To facilitate expression of multiple MHCI in recipient liver, we created a construct in which the 3 d-haplotype heavy chains Dd, Ld and Kd were separated by an F2A linker (DaLeK), and then determined the effect of administration of this vector upon heart graft survival.

Methods: DaLeK was packaged into a liver-specific rAAV2/8 vector. Fully-allogeneic hearts from DBA/2 (H-2b) were transplanted into C57BL/6 (H-2d) at either d7 or d14 postinoculation.

Results: Administration of 5x10^11 vector genome copies AAV-DaLeK to C57BL/6 mice yielded strong expression of Dd, Ld and Kd on hepatocytes. Expression was enhanced by co-transduction with a vector encoding β2 microglobulin, ALT levels remained normal and no inflammatory infiltrates were detected. Survival of DBA/2 hearts transplanted into AAV-DaLeK treated mice was prolonged from a MST of 7 days to 23 days. Administration of a control vector did not alter survival (figure).

Conclusion: AAV-DaLeK permits expression of multiple MHCI from a single vector, and its administration significantly prolongs survival of fully-allogeneic heart transplants. A combination of AAV-DaLeK with vectors expressing CIITA and/or allogeneic MHC class II may produce tolerance to fully-allogeneic grafts.

Survival of DBA/2 to C57BL/6 transplants - DaLeK

FIGURE 1.
CAN EXPRESSION OF ALLOGENEIC MHC CLASS II IN RECIPIENT LIVER INDUCE REGULATORY TRANSPLANTATION TOLERANCE?

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Background: Regulatory tolerance to allogeneic cardiac grafts after donor MHC II gene transfer to recipient bone marrow is reported. Allogeneic MHC II is strongly expressed in recipient liver following AAV-mediated gene transfer, accompanied by a dose-dependent increase in liver Tregs. However, survival of allogeneic heart grafts in transduced recipients is unchanged. Hepatocytes are not professional APC, lacking significant expression of co-stimulatory molecules, and chaperones required for antigen processing and presentation.

To determine whether augmenting expression of molecular chaperones and/or co-stimulatory molecules by hepatocytes would facilitate induction of allograft tolerance.

Method: C57BL/6 mice received 1x10¹¹vgc AAV2/8 encoding Class II transactivator (CIITA) and 5x10¹¹vgc IA⁵ or IA⁵ alone. MHC II, co-stimulatory molecules, chaperones and inflammatory infiltrate were assessed. IA⁵-binding peptides eluted from livers expressing IA⁵ alone or IA⁵/CIITA, were identified by mass spectrometry. DBA/2 hearts were transplanted at d7 or d30 postinoculation.

Results: CIITA transduction upregulated expression of native IA⁵. Expression of H-2M α and β and of Invariant chain were increased 70 to 500-fold by CIITA, attaining levels comparable to those in spleen. Peptides eluted in the presence of CIITA conformed to the IA⁵-binding motif (Figure). Expression of co-stimulatory molecules on hepatocytes was not increased by CIITA. Survival of DBA/2 grafts was not altered by the addition of CIITA to IA⁵.

Conclusion: Expression of CIITA and a single mismatched MHC II in hepatocytes was not sufficient to confer tolerance to fully-allogeneic heart grafts. Ongoing experiments are evaluating the combination of 2 mismatched MHC II and/or CD86 with CIITA.

FIGURE. peptides eluted from livers expressing both IA⁵ and CIITA conform to the IA⁵-binding motif at anchor residues P1, P4, P6 and P9.
INNATE ALLO-RECOGNITION RESULTS IN RAPID ACCUMULATION OF MONOCYTE DERIVED DENDRITIC CELLS

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Background: Monocyte derived dendritic cells (moDCs) are rare in the steady state but accumulate during infection and inflammation. They are involved in innate and adaptive immune responses in various conditions; however how they are evoked in response to allogeneic stimuli is poorly understood.

Methods: In mice on the C57BL/6, BALB/c, DBA/2 and NOD genetic backgrounds, we enumerated splenic moDCs and conventional dendritic cells (cDCs), following adoptive transfer of syngeneic or allogeneic splenocytes, and compared them to untreated mice.

Results: moDCs became abundant 1 day after IV injection of allogeneic splenocytes but not syngeneic splenocytes, while cDC numbers were unaffected by either allogeneic or syngeneic stimulation. This occurred in various donor-host strain combinations. Using cells from MHC-matched DBA/2 and BALB/c mice, we found that allogeneic moDC induction did not require MHC mismatch. The potency of allogeneic moDC induction was dependent on the number of donor cells transferred and could be induced by various donor cell types including B cells, T cells or natural killer (NK) cells. Using cells from lymphoid cell-deficient RAG2-/-γc-/- and NOD-scid-IL2Rγc-/-; and selectively NK-deficient Mcl1fl/flNcr1-Cre mice, we found that allogeneic moDC induction only occurred in the presence of either host or donor lymphoid cells, particularly NK cells.

Conclusion: moDCs accumulate rapidly following exposure to allogeneic antigen. This process requires the presence of either host or donor lymphoid cells, and occurs independently of MHC mismatch. This innate allo-recognition raises potential new insights into how the immune system responds to allogeneic encounters such as that which occurs during organ transplantation.

Sensitisation, Antibodies and ABO Incompatible Transplantation & Organ Donation and Ethics

PROVIDING BETTER MATCHED DONORS FOR HLA MISMATCHED COMPATIBLE PAIRS THOUGH KIDNEY PAIRED DONATION

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Background: To define allocation metrics that enable compatible pairs (CP) receiving a better-matched kidney in kidney paired donation (KPD) program, without disadvantage to incompatible pairs (ICP).

Participation of CP in KPD could be attractive to CP who have a high degree of HLA-mismatch, if the KPD allocation algorithm provides a better HLA match for the CP recipient. Because KPD programs were not designed to help CP, it is important to define allocation metrics that enable CP receiving a better-matched kidney, without disadvantage to ICP.

Methods: Virtual crossmatch is used for ICP allocation in the Australian KPD program. The algorithm ignores HLA matching rules and therefore is unlikely to provide better HLA matching to CP. Simulations using 46 ICP and 11 randomly selected CP with 6/6 ABDR mismatch were undertaken. Allocations were preformed adding 1 CP at a time or all 11 CP at once, without and with exclusion of unacceptable antigens selected to give a virtual cPRA in the range of 70-80% to improve HLA matching in CP recipients.

Results: Inclusion of 1 CP at a time increased matching in ICP by up to 33% and inclusion of all 11 CP at once increased ICP matching by 50%. The difference in the average eplet mismatch (EpMM) with the own donor (78±19) was significantly lower (57±15, P<0.02) only when individual CP recipients had unacceptable antigens assigned for exclusion. When the 11 CP were added at once the EpMM with the matched donor was significantly better than with the own donor when they were added without (58±10, P<0.03) and with (60±11, P<0.02) exclusion of unacceptable antigens. Only recipients whose EpMM to own donor was >65 significantly reduced the EpMM with the matched donor.

Conclusions: CP participation in KPD can increase match rates in ICP and can provide a better immunological profile in CP recipients who have a high EpMM to their own donor when using allocation based on virtual crossmatch.
SYK INHIBITION REDUCES RENAL ALLOGRAFT INJURY IN A RAT MODEL OF ACUTE ANTIBODY-MEDIATED REJECTION IN HIGHLY SENSITIZED RECIPIENTS

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Background: To determine the therapeutic potential of Syk inhibition in a rat model of antibody-mediated renal allograft rejection in sensitized recipients.

Methods: Recipient Lewis rats were immunized with donor (Dark Agouti) spleen on day-5. Recipients underwent bilateral nephrectomies and orthotopic renal transplantation (day 0). Groups received Syk inhibitor (SYK-A, 30mg/kg/bid)(n=11) or vehicle(n=12) from -1hr until being euthanized on day 3. Cellular rejection was minimized by administration of the IL-2 inhibitor, Tacrolimus, given from day -1.

Results: Vehicle treated recipients exhibited delayed graft function on day 1(serum creatinine 230±84 μmol/L vs 45±5 μmol/L normal) which worsened by day 3(363±192 μmol/L). Histology showed severe damage (thrombosis, acute tubular injury, capillaritis). High serum levels of donor-specific antibodies were detected by flow cytometry and rat IgG and C3 were deposited in allografts. A modest T cell infiltrate was evident, but little up-regulation of IL-2 mRNA, indicating effective Tacrolimus inhibition of cellular rejection. SYK-A did not prevent delayed graft function on day 1, but significantly improved graft function on day 3(199±131 μmol/L; P<0.05 vs vehicle) with reductions in capillaritis, tubular injury and thrombosis. Immunostaining showed a 45% reduction in the macrophage infiltrate (P<0.05), and an 80% reduction in IFN-γ mRNA levels in the Syk inhibitor treated animals suggesting reduced macrophage activation. T cell infiltration, IL-2 mRNA levels and serum DSA levels were equivalent to levels observed in the vehicle treated group.

Conclusions: Syk inhibition significantly attenuated allograft injury in a model of severe antibody-mediated damage in highly sensitized recipients. These findings suggest Syk inhibition as a potential adjunctive treatment in clinical AMR.

THE NATURAL HISTORY OF DONOR SPECIFIC ANTIBODIES (DSA) IN KIDNEY TRANSPLANT RECIPIENTS (KTX) AND ASSOCIATED CLINICAL OUTCOMES

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Background: DSA are implicated in the development of rejection and graft dysfunction. However, the natural history remains poorly characterized.

To characterize DSA development and associations with clinical outcomes in KTx.

Methods: Serum samples from adult KTx between July2010-May 2015 were prospectively collected pretransplant and at Days 7, 28 and Months 3, 6, 9, 12 posttransplant and tested for DSA on a luminex platform. Acute rejection (AR) episodes were biopsy proven.

Results: 122 recipients had pre and posttransplant DSA testing. Mean follow-up was 29±15 months. Seventy (57%) patients had DSA; 48 (39%) had preexisting DSA only, 10 (8%) had denovo (dn) DSA only, and 12 (10%) had preexisting and dnDSA. Of patients with dnDSA; 7(32%) had ClassI antibodies only, 12(55%) had ClassII antibodies only and 3(14%) had Class I&II. Twenty-four (40%) patients with preexisting DSA and 14 (64%) patients with dnDSA had AR. Patients with dnDSA vs those without were more likely to develop AR (OR4.75; 95%CI 1.64-13.75; P=0.004), however there was no increased risk in patients with preexisting DSA only (OR1.36; 95%CI 0.58-3.20; P=0.485). Median time to rejection was 2.3 months (IQR0.2-7.4). dnDSA appeared prior to the rejection episode in all patients with dnDSA and AR. Mean creatinine at 6 and 12 months posttransplant was higher in patients with dnDSA vs without dnDSA (Mean 12-month creatinine: 171 vs 128 μmol/L; t83=-3.33; P=0.001).

Conclusions: 18% of patients developed dnDSA. This was associated with a higher risk of AR and worse graft function. Further evaluation of the risk factors for dnDSA and the association with long-term outcomes is required.
ADDITIONAL OPPORTUNITIES FOR TRANSPLANTING ORGANS FROM DONORS WITH BRAIN MALIGNANCIES? AN AUDIT OF THE NSW ORGAN AND TISSUE DONATION SERVICE (OTDS) ORGAN DONOR REGISTER

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Background: Donors with primary brain malignancies (PBM) present an on-going challenge due to uncertainty around transmission risk, classification complexity and variability in guidelines. Data for donors who don’t proceed is not captured by ANZOD. We sought to retrospectively identify any untapped potential opportunities for organ donation among people with PBM referred to the NSW OTDS.

Methods: We reviewed all NSW OTDS referral logs for 2010-2015. We compared people with past/current PBM who donated (actual/intended) and did not donate (potential donors), including those deemed not medically suitable due to cancer, in light of current evidence. Reasons for outcome variability were evaluated.

Results: Of 2,611 total donation referrals (2,032 potential, 579 intended/actual), 49 patients had PBM, 10 of whom donated (7 actual, 3 intended) and 39 who did not (21 excluded due to PBM) (Table). Those who donated had lower grade tumours, while patients excluded due to PBM were more likely to have higher grade tumours or unclear grading. Medical suitability decisions were variable for astrocytoma and meningioma. We identified 19 additional potential donor opportunities, including 3 people with PBM of ‘low’ transmission risk (<2%) (2 astrocytoma, meningioma). A further 16 people had ‘intermediate’ transmission risk (2.2% with an upper 95% CI of 6.4%) malignancies (glioblastoma, germinoma, ependymoblastoma).

Conclusions: Realisation of an additional potential 19 donors would increase intended/actual donor pool by 3.3%. Limitations in administrative data mean all considerations informing past decisions may not be clear. Further consideration of the potential for people with PBM, including higher grade tumours, to be donors may be warranted.

<table>
<thead>
<tr>
<th>Type of primary brain malignancy</th>
<th>Tumour grading</th>
<th>Estimated transmission risk (upper 95% CI)</th>
<th>Potential (NMS due to cancer)</th>
<th>Actual and Intended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acoustic neuroma</td>
<td>Low</td>
<td>&lt;2%</td>
<td>3 (2)</td>
<td>2</td>
</tr>
<tr>
<td>Astrocytoma</td>
<td>Variable</td>
<td>&lt;2%</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
<td>Low</td>
<td>&lt;2%</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ependymoblastoma</td>
<td>High</td>
<td>2.2% (6.4%)</td>
<td>1(1)</td>
<td></td>
</tr>
<tr>
<td>Ganglioma</td>
<td>Low</td>
<td>&lt;2%</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Glioma/Glioblastoma/ Glioblastoma multiforme</td>
<td>High</td>
<td>2.2% (6.4%)</td>
<td>18 (14)</td>
<td></td>
</tr>
<tr>
<td>Medulloblastoma (past cancer, deemed cured)</td>
<td>High</td>
<td>N/A</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Meningioma</td>
<td>Variable</td>
<td>&lt;2%</td>
<td>9 (2)</td>
<td>3</td>
</tr>
<tr>
<td>Thalamic germinoma</td>
<td>High</td>
<td>2.2% (6.4%)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td>Unspecified Cerebral</td>
<td>N/A</td>
<td>N/A</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>39 (21)</td>
<td>10</td>
</tr>
</tbody>
</table>

1. Tumour grades obtained from OTDS registry records, with WHO Grading of Tumours of the Central Nervous System guideline used where grades were not recorded. 2. Estimated transmission risks were obtained from SBTO Advisory Committee on the Safety of Blood, Tissues and Organs, Transplantation of Organs from Deceased Donors with Cancer or a History of Cancer, UK, 2014.
NSW donor referrals from 2010–2015 not proceed is not captured by ANZOD. We sought to describe

**Background:** Data for people referred for organ donation who do not proceed is not captured by ANZOD. We sought to describe NSW donor referrals from 2010–2015 with hepatitis C (HCV), hepatitis B (HBV) and human immunodeficiency virus (HIV) who did not donate (potential donors), including those deemed not medically suitable (NMS) due to behaviours that are high risk for BBVs. Reasons for outcome variability were evaluated.

**Methods:** We reviewed NSW Organ and Tissue Donation Service referral logs for 2010–2015. We reviewed referrals with BBVs (hepatitis B, C and HIV) who donated (actual/intended donors) and did not donate (potential donors), including those deemed not medically suitable (NMS) due to behaviours that are high risk for BBVs. Reasons for outcome variability were evaluated.

**Results:** Of 2,611 total donation referrals (2,032 potential, 579 intended/actual), 151 (5.8%) were recorded as having BBVs, 124 of these with HCV, 25 with HBV (table). There were 135 potential BBV donors and, 16 actual/intended donors (10.6% of referrals with BBVs). For 37 (24.5%) of referrals with BBVs no suitable recipient was found. None of the 5 patients with HIV became actual donors. Among the 135 potential BBV donors, consent was not granted (family or coronial refusal) in 32 cases, 23 were deemed NMS due to high risk behaviour, and 66 were NMS for reasons unrelated to BBVs.

**Conclusions:** In NSW, referrals with BBVs are considered for and in certain circumstances proceed to organ donation. With potentially curative treatments for HCV imminent, new risk paradigms may evolve. Consideration of opportunities to increase donation rates, particularly among those identified as high risk for BBV transmission, may be warranted.

**TABLE.**

Donors with blood borne viruses by donation outcome in NSW, January 2015 to June 2015

<table>
<thead>
<tr>
<th>Blood borne virus</th>
<th>Total donors</th>
<th>Potential donors</th>
<th>Actual &amp; intended donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B virus (HBV)</td>
<td>13</td>
<td>12 (3)</td>
<td>1</td>
</tr>
<tr>
<td>Hepatitis C virus (HCV)</td>
<td>112</td>
<td>99 (15)</td>
<td>13</td>
</tr>
<tr>
<td>HBV + HCV</td>
<td>12</td>
<td>12 (3)</td>
<td>0</td>
</tr>
<tr>
<td>Unspecified hepatitis</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Possible hepatitis</td>
<td>6</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>HIV</td>
<td>5</td>
<td>4 (2)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>151</strong></td>
<td><strong>135 (23)</strong></td>
<td><strong>16</strong></td>
</tr>
</tbody>
</table>

* In total, 56 of 2,611 total referrals were deemed NMS due to ‘high risk’ behaviour, including the 23 with identified BBVs noted above.
SUCCESSFUL ABO INCOMPATIBLE NONHEART BEATING DECEASED DONOR KIDNEY TRANSPLANTATION
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Background: Deceased donor kidney allocation is conventionally made by ABO acceptable criteria. Western Australia (WA) does not ship donation after circulatory death (DCD) kidneys due to concerns with prolonged cold ischaemic time. To maximize allocation and overcome the difficulty in allocating DCD kidneys within blood groups A, B and AB due to low numbers of potential recipients, WA devised a strategy to ensure DCD allocation could occur regardless of ABO blood group by measuring Anti-A and B titres on waitlisted patients.

Methods: We report 2 cases of DCD transplantation where nonavailability of appropriate blood group matched recipient in WA required implementing ABO-incompatible (ABOi) transplantation. 

ADPCKD = Autosomal dominant polycystic kidney disease *Anti-A column # conventional PEx.

Both patients received preoperative plasmapheresis and induction with rabbit anti-thymocyte globulin or basiliximab, with reduction in pretransplant anti-A titres to 1:4 or less.

Results: Though their courses were complicated by delayed graft function, creatinine improved to nadir of 130 μmol/L and 165 μmol/L respectively, with early protocol biopsies showing no cellular or humoral rejection. To our knowledge, patients 1 and 2 are the first deliberate ABOi DCD and ABOi ECD DCD performed in Australia.

Conclusion: Local allocation of ABOi DCD donors is a viable option to allow renal transplantation, avoiding prolonged ischaemic time from shipping or organ discard due to no ABO acceptable recipient.

TREATMENT OF ACTIVE ANTIBODY MEDIATED REJECTION IN RENAL TRANSPLANT RECIPIENTS
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Department of renal transplantation surgery, Toranomon Hospital Kajigaya

Background: To evaluate the adequacy of our treatments for active antibody mediated rejection (aAMR) in renal transplant recipients based on the outcome.

Methods: Out of 120 recipients from 2007 to 2015 at our hospital, biopsy proven aAMR cases were identified and examined about patient background, immunological risk, pathological finding, treatment and outcome.

Results: Four early onset aAMR (E-group) and 6 late onset aAMR (L-group) were diagnosed with biopsy, of which 4 cases (2 E-group and 2 L-group) were not fulfilled Banff criteria but considered as aAMR. All cases had deterioration of graft function. Treatment for aAMR included bolus steroid (all), IVIG (all), Deoxyspergualin (4/9), and plasma exchange (PE) (6/9). None of them was applied Rituximab after diagnosis of aAMR, but 2 cases had this prior to the operation due to ABO incompatible transplantation. Mean follow-up period after diagnosis were 2.0 years (range 0.3-7 years), and 1 graft was lost in E-group. Mean creatinine level was 2.2 mg/dl (range 1.2-5.0 mg/dl). Three cases of E-group were complicated at diagnosis and 1 of them did not receive PE resulting in graft loss, whilst others with severe renal dysfunction had PE immediately. On a case of L-group due to difficult pathological findings PE was hesitated for 2 years after biopsy, then his graft function worsen in the meantime.

Conclusions: With short term follow-up most of aAMR could have been managed with these treatments. Our experience suggested that just-in-time treatment including PE might improve the aAMR patients’ outcome especially in complicated pathological finding cases.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/Gender</th>
<th>Renal Disease</th>
<th>Donor age/Gender</th>
<th>Recipient blood group</th>
<th>Donor blood group</th>
<th>Anti-A titre pre</th>
<th>Anti-A titre post</th>
<th>Total ischaemic time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54/F</td>
<td>ADPCKD</td>
<td>63/M</td>
<td>B</td>
<td>A2</td>
<td>1:16</td>
<td>1:2#</td>
<td>7:25</td>
</tr>
<tr>
<td>2</td>
<td>66/M</td>
<td>ADPCKD</td>
<td>65/F</td>
<td>B</td>
<td>A1</td>
<td>1:8</td>
<td>1:4#</td>
<td>7:36</td>
</tr>
</tbody>
</table>
ALLOGRAFT DYSFUNCTION COMPLICATING PARATHYROIDECTOMY IN RENAL TRANSPLANT RECIPIENTS: A TYPICAL CASE AND REVIEW OF THE LITERATURE ON UNDERLYING MECHANISM

SEE Emily1, and DWYER Karen2
1Department of Nephrology, Barwon Health, 2School of Medicine, Deakin University

Background: Persistent hyperparathyroidism after successful renal transplantation is a common clinical problem. Deterioration in renal allograft function following parathyroidectomy is recognised, however the mechanism underpinning this decline is not well described. We present a typical case and a review of the literature surrounding the pathogenesis.

Methods: A 60 year-old male underwent living unrelated renal transplantation for ESKD secondary to IgA nephropathy. He underwent subtotal parathyroidectomy 6-months later due to persistent tertiary hyperparathyroidism. His creatinine immediately rose from 170 to 270umol/L. Renal biopsy demonstrated medullary calcium deposition and mild CNI toxicity. His creatinine improved to 200umol/L after several months where it has remained for 5 years.

Results: Evidence from preclinical studies suggests that PTH has a regulatory effect on renal perfusion, glomerular filtration and mesangial cell function. By mimicking the vascular action of PTHrP, elevated levels of circulating PTH result in vasodilatation of the renal artery, preglomerular arterioles and glomeruli leading to augmented renal perfusion and glomerular filtration. In human studies, infusions of PTH/PTHrP result in a dose-dependent increase in renal blood flow as well as enhanced cardiac output. Therefore, a rapid decline in circulating PTH unsurprisingly results in an acute reduction in graft perfusion. This reduction may be further augmented by the vasoconstrictive effect of calcineurin inhibitors.

Conclusion: Hyperparathyroidism following renal transplantation poses a complex clinical problem. Alterations in renal blood flow and microcirculation have deleterious effects on graft function although fortunately do not affect graft survival. Ultimately, this reinforces the necessity for optimisation of biochemical parameters prior to transplantation.

ANTI BLOOD GROUP ANTIBODY TITRES IN BLOOD GROUP A AND B TRANSPLANT WAIT LISTED PATIENTS

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1Nephrology and Renal Transplant, Royal Melbourne Hospital, 2Renal & Transplantation Unit, Royal Melbourne Hospital, 3School of Medicine, Monash University, Melbourne, 4Department of Medicine, University of Melbourne

Background: Historically, deceased donor ABO-incompatible renal transplantation (DD-ABOi) has been limited to kidneys from A2 or A2B blood group donors transplanted into group B recipients with low anti-A titres. Recent successful living donor ABOi from all blood groups into recipients with low titre anti-blood group antibody (ABGAb) using standard immunosuppression alone suggests DD-ABOi may be possible into selected recipients with limited or no antibody removal pretransplantation. We sought to systematically measure ABGAb titres in our deceased donor wait listed group A and B patients.

Methods: ABGAb titres of wait listed patients were compared with our institutional threshold for transplantation of ≤1:8 (Ortho) to determine how many might accept a DD-ABOi kidney with 1 or no antibody removal treatments prior to transplantation.

Results: To date 36/106 (34%) group A and 16/55 (29%) group B patients have had titres measured. Of the group A patients, 66% had an anti B titre ≤1:8 with 69% of group B patients having an anti A titre ≤1:8. Of the 52 patients who have had titres measured, 25 (48%) have titres <1:4.

Conclusion: A significant number patients have ABGAb sufficiently low to enable DD-ABOi with limited or no antibody removal.
BENEFITS OF MODERATING LOCATION OF DONOR LIFE SUPPORT WITHDRAWAL ON LIVER TRANSPLANTATION USING DONATION AFTER CIRCULATORY DEATH: A META-ANALYSIS

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1Transplantation Laboratory, Victor Chang Cardiac Research Institute, Sydney, 2Western Clinical School, Westmead Hospital, Sydney, 3Australian National Liver Transplantation Unit, Royal Prince Alfred Hospital, Sydney, 4Institute of Academic Surgery, Royal Prince Alfred Hospital, Sydney, 5Department of Surgery, Westmead Hospital, Sydney

Background: Prolonged warm ischaemic time, and the associated micro-thrombi formation, have been identified as the key factors responsible for poor outcomes of liver transplantation using donation after circulatory death (DCD) compared to using donation after brain death (DBD). Therefore, we sought to investigate the effects of ante-mortem heparin administration and location of donor life support withdrawal in intensive care unit (ICU) vs. operating theatre (OT) on DCD outcomes.

Methods: Medline, EMBASE and Cochrane libraries were systematically searched and 23 relevant studies identified for analysis.

Results: Donor life support withdrawal in OT, compared to ICU, was associated with reduced DCD patient mortality (OT: OR = 1.2, 95% CI 0.85-1.68; ICU: OR = 2.15, 95% CI 1.15-4.02), graft loss (OT: OR = 1.65, 95% CI 1.16-2.36; ICU: OR = 1.98, 95% CI 1.13-3.47) and incidence of ischaemic cholangiopathy (OT: OR = 13.73, 95% CI = 5.18-36.44; ICU: OR = 19.68, 95% CI 7.48-51.75) relative to DBD recipients. Ante-mortem administration of heparin attenuated the rate of allograft primary nonfunction (heparin: OR = 3.48, 95% CI 1.79-6.76; no heparin: OR = 11.24, 95% CI 1.99-63.37).

Conclusions: Our evidence suggests that these changes in DCD donor life support withdrawal could confer significant benefits upon their recipients. Specifically the practice of using ante-mortem heparin and withdrawal of treatment in the OT could reduce rate of graft and patient loss, and ischaemic cholangiopathy, thereby maximising benefits derived from these valuable organs.

RISK OF HEPATITIS B REACTIVATION IN CORE ANTIBODY POSITIVE PATIENTS AFTER RENAL TRANSPLANTATION

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1Princess Alexandra Hospital, Brisbane, 2Department of Gastroenterology, Princess Alexandra Hospital, Brisbane, 3Department of Nephrology, Princess Alexandra Hospital, Brisbane, 4School of Medicine, University of Queensland at the Princess Alexandra Hospital

Background: Reactivation of Hepatitis B virus (HBV) post transplantation may cause severe acute hepatitis. The risk of HBV reactivation in HBV core antibody positive (HepBcAb+) and HBV surface antigen negative (HepBSAg-) renal transplant recipients (RTR) is unknown. Following an index case of HBV reactivation, practice at our centre was evaluated.

Methods: Retrospective cohort study of RTR transplanted between 1970–2014. HBV status was recorded and HepBcAb+, HepBSAg– patients had HBV serology and quantitative DNA measured.

Results: Of 740 patients studied, 692 had HBV status evaluated, 11 patients were HepBSAg positive at transplant and treated with antiviral agents. 57 (8.2%) patients were HepBcAb+, HepBSAg - at transplant. Twenty nine (50%) were Asian, thirteen (23%) were Pacific Islander. Median time from transplant was 7.6y. Two patients were preemptively treated with anti-viral therapy. No systematic screening for HBV seroreversion was undertaken. On rescreening, 4 had detectable HBV DNA (including index case) ranging from 1.9 x 10^2 to >1.1x 10^8 IU/ml. Two patients had mild derangements of liver function tests (ALT < x2 ULN). Liver ultrasound was mildly abnormal in 3. At transplant, HepBSAb was < 100 in 3 of 4 patients.

Conclusions: We found a low rate of HBV reactivation in cAb positive RTR which was not associated with clinically significant disease. Patients undergoing renal transplantation should be screened prior to transplant for HBV and standardised protocols for monitoring HBV status should be implemented (such as annual HepBSAg testing) however preemptive antiviral therapy does not appear to be warranted.
SUBCLINICAL CYTOMEGALOVIRUS VIRAEMIA IN RENAL TRANSPLANT RECIPIENTS

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¹Renal Transplant Unit, Austin Hospital, Melbourne, ²Renal Transplant Unit, Monash Medical Centre, Melbourne

Background: Studies suggest low-level cytomegalovirus (CMV) viraemia, detected with sensitive molecular assays, may lead to poorer graft outcomes following renal transplantation. Investigate the incidence, outcomes, and clinical associations of subclinical CMV viraemia in adult renal transplant recipients.

Methods: A retrospective cohort study from January 2010 to March 2012 with 3 years follow up.

Results: 22/59 patients were diagnosed with subclinical viraemia. 8/22 cases occurred whilst receiving anti-viral prophylaxis. Renal function was similar at 12, 24 and 36 months in both CMV viraemic and nonviraemic patients. Total rejection was not different (P = 0.13) between groups. Anti-viral prophylaxis was under-dosed when corrected for GFR at day 7 in 83.3% of patients who developed viraemia on prophylaxis, compared to 23.1% of patients with viraemia after prophylaxis stopped and 22.7% of patients who were never viraemic (P = 0.03). By 21 days there was no significant difference in prophylaxis dosing between groups. In those who developed CMV during prophylaxis the percentage improvement in GFR at 14 to 28 days was 161.7% compared to 49.7% in the CMV after prophylaxis and 36.3% in the never viraemic group P = 0.001. Median time on dialysis post transplant was higher in those who later developed subclinical viraemia P = 0.01 (Figure).

Conclusion: Subclinical CMV viraemia is common and associated with early dialysis requirements following transplantation. Early under-dosing of antiviral prophylaxis was significantly associated with rapid improvement in GFR and a risk factor for subclinical CMV during the prophylaxis period. Accurate early prophylaxis dosing and CMV surveillance may benefit patients with delayed graft function.

CRYPTOCOCCAL INFECTIONS IN SOLID ORGAN TRANSPLANT RECIPIENTS OVER A 15 YEAR PERIOD IN QUEENSLAND

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¹Department of Infectious Diseases, Princess Alexandra Hospital, Brisbane, ²Department of Nephrology, Princess Alexandra Hospital, Brisbane, ³Queensland Renal Transplant Service, Princess Alexandra Hospital, Brisbane

Background: To determine the incidence, risk factors and clinical outcome of solid organ transplant recipients diagnosed and treated for cryptococcosis at Princess Alexandra Hospital in Brisbane.

Methods: Retrospective analysis of all patients with solid organ transplant (SOT) diagnosed and treated for cryptococcal infection occurring between January 2001 and December 2015.

Results: Of 102 patients diagnosed with cryptococcal infection, 21 were SOT recipients. Renal transplant accounted for 20/21 cases. The annual incidence of infection has risen significantly, and is now greater than 2/1000 prevalent renal transplant recipients. There was no statistically significant difference between meningitis vs. nonmeningitis cohorts with regards to patient demographic, clinical presentation or treatment outcomes.

Conclusion: Cryptococcal infection in solid organ transplant recipients remains rare, however there has been a marked increase in incidence since 2014. This study reveals a need for increased vigilance for a potential emerging infectious disease. It further highlights the need for ongoing research in order to further aid diagnosis, management and prognostication.
EXTENDED PROPHYLAXIS WITH VALGANCICLOVIR REDUCES THE INCIDENCE OF CYTOMEGALOVIRUS DISEASE IN RENAL TRANSPLANT RECIPIENTS

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1Department of Medicine, Royal Melbourne Hospital, 2Department of Nephrology, Royal Melbourne Hospital, 3Department of Nephrology, Western Hospital

Background: Cytomegalovirus (CMV) disease is the commonest life-threatening opportunistic infection following renal transplantation, remaining a major source of morbidity, despite regimens aimed at preventing disease.

Methods: Here we report CMV outcomes in 469 consecutive patients undergoing renal transplantation from 2004 to 2009 following adoption of a protocol in which valganciclovir prophylaxis was extended to 6 months for seronegative recipients receiving kidneys from seropositive donors (D+/R-), and 3 months for D+/R+ and D-/R+.

Results: Over 90% received tacrolimus/mycophenolate/prednisolone based immunosuppression with CMV disease occurring in 14 patients (3%) at a median 248 days posttransplant: 8 of 63 D+/R- (12.7%), 4 of 229 D+/R+ (1.7%), 1 of 95 D-/R+ (1.1%) and 1 of 82 D-/R- (1.2%). Of these 14 patients, 6 had received additional immunosuppression for rejection, and 1 had received additional high dose steroid for recurrent FSGS. By comparison, in 203 patients transplanted from 2000 to 2004 when prophylaxis was restricted to D+/R- & consisted of 3 months of valaciclovir and 2 months CMV immunoglobulin (CMVIg) 21 patients developed CMV disease (10.3%) at a median of 125 days post-transplant: 10 of 46 D+/R- (21.7%), 9 of 103 D+/R+ (8.7%), 1 of 32 D-/R+ (3.1%), 1 of 22 D-/R- (4.5%), P < 0.001 (Table 1). Extending valganciclovir prophylaxis to 6 months in D+/R- and 3 months for D+/R+ and D-/R+ reduced the incidence of CMV disease compared to the previous valaciclovir based regimen.

Conclusions: These results also compare favourably to recent published series and may additionally reflect exposure to lower levels of immunosuppression.

<table>
<thead>
<tr>
<th>TABLE 1. CMV disease within D/R subgroups, comparing current and previous prophylaxis regimens</th>
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<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>D+/R-</td>
</tr>
<tr>
<td>D+/R+</td>
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<tr>
<td>D-/R+</td>
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<tr>
<td>D-/R-</td>
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</table>

OBESITY IS A RISK FACTOR FOR CMV DISEASE IN RENAL TRANSPLANT RECIPIENTS RECEIVING EXTENDED PROPHYLAXIS WITH VALGANCICLOVIR

STRAW SC1, HUGHES P2, MASTERSON R2, and COHNEY S1,3
1Department of Medicine, Royal Melbourne Hospital, 2Department of Nephrology, Royal Melbourne Hospital, 3Department of Nephrology, Western Hospital

Background: Cytomegalovirus (CMV) disease remains a major source of morbidity with potentially fatal consequences despite a number of regimens aimed at prevention. Historically, a variety of risk factors have been identified including donor age, rejection episodes and impaired transplant function, though the major risk factors remain the extent of immunosuppression and the CMV serostatus of donor (D) and recipient (R).

Methods: In this study, we examined risk factors for CMV disease amongst 469 consecutive ESKD patients undergoing renal transplantation from 2004 to 2009 managed according to a protocol in which CMV prophylaxis with valganciclovir was 6 months for D+/R- and 3 months for D+/R+ & D-/R+. More than 90% of patients received a regimen based on tacrolimus, mycophenolate and prednisolone.

<table>
<thead>
<tr>
<th>TABLE 1. Baseline characteristics</th>
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<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Age, Mean ± SD</td>
</tr>
<tr>
<td>Weight at Transplant (kg), mean ± SD</td>
</tr>
<tr>
<td>Aetiology of renal disease</td>
</tr>
<tr>
<td>GN</td>
</tr>
<tr>
<td>DM</td>
</tr>
<tr>
<td>Hypertensive</td>
</tr>
<tr>
<td>Polycystic</td>
</tr>
<tr>
<td>Reflux</td>
</tr>
<tr>
<td>Interstitial nephritis</td>
</tr>
<tr>
<td>Obstructive</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Number of grafts</td>
</tr>
<tr>
<td>&gt;1 graft</td>
</tr>
<tr>
<td>Donor source</td>
</tr>
<tr>
<td>Cadaveric</td>
</tr>
<tr>
<td>CMV D/R status</td>
</tr>
<tr>
<td>D+/R-</td>
</tr>
<tr>
<td>D+/R+</td>
</tr>
<tr>
<td>D-/R+</td>
</tr>
<tr>
<td>HLA mismatches</td>
</tr>
<tr>
<td>Ave total mismatches ± SD</td>
</tr>
</tbody>
</table>
Results: CMV disease occurred in only 3% of patients (14 of 469), with a rate of 12.7% amongst D+/R-. As expected CMV disease was more common in D+/R-, following treatment for rejection, and occurred in 2 out of 6 patients receiving the janus kinase 3 inhibitor (Jak3i) tofacitinib. None of the 25 patients receiving mTOR inhibitors developed CMV disease. Additional risk factors were number of HLA mismatches, and weight prior to transplant (Table 1).

Conclusions: Despite low rates of CMV disease with this prophylaxis protocol, HLA mismatches, rejection and pretransplant weight remain as significant risk factors for CMV disease. This provides an additional reason to counsel patients to lose weight prior to transplantation.

CMV disease is not associated with any increase in graft loss or mortality in renal transplant recipients receiving extended prophylaxis with valganciclovir

Background: Cytomegalovirus (CMV) disease is the commonest life-threatening opportunistic infection following renal transplantation. It has remained a major source of morbidity and mortality despite various regimens to prevent disease. In 2004, a protocol was adopted in which CMV prophylaxis was extended to 6 months valganciclovir for seropositive donor (D+) to seronegative recipient (R-), and 3 months for D+/R+ & D-/R+.

Results: Amongst 469 consecutive renal transplant recipients managed according to this regimen from 2004 to 2009, CMV disease occurred in 14 patients (3%) at a median 248 days posttransplant, with 7 developing organ specific disease and the remainder vague systemic symptoms. Three were managed as outpatients, while amongst those hospitalised, median length of stay was 5 days (average 8.6 days). One patient required ICU. At a median 1556 days following CMV disease (average 1455), graft loss was 4/14 (28.6%) in patients who experienced CMV disease and 78/455 (17.1%) in those remaining CMV free (p = 0.281). Subsequent mortality was 2/14 (14.3%) in those with CMV disease and 17/455 (3.7%) in those without (p = 0.106). In 1 of the 2 deaths in the CMV group, CMV viraemia was an intercurrent event in a patient dying from alcoholic liver disease and pancreatitis.

Conclusions: Thus, in patients receiving "extended" valganciclovir prophylaxis (6 months in D+/R-, 3 months for D+/R+ and D-/R+) CMV disease was associated with only short hospital stays and was not associated with an increased rate of graft loss or mortality.
CMV SEROSTATUS, PATIENT AND ALLOGRAFT SURVIVAL AND PATTERNS OF CMV PROPHYLAXIS IN AUSTRALIAN AND NEW ZEALAND KIDNEY TRANSPLANT RECIPIENTS.

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1Centre for Kidney Research, The Children’s Hospital at Westmead, Sydney, 2Auckland Renal Transplant Group, Auckland City Hospital, 3Department of Renal Medicine, Sir Charles Gairdner Hospital, Perth

Background: CMV syndrome and disease is the commonest opportunistic infection after kidney transplantation although whether CMV serostatus is associated with survival is controversial.

We aimed to determine the association between donor and recipient CMV serostatus and patient survival and to investigate the use of CMV prophylaxis within the ANZ kidney transplant population.

Methods: All adult (age > 18 years) transplant recipients who received their first deceased donor kidney transplants between 1990 and 2012 were included. We examined cause specific and all-cause mortality according to CMV donor and recipient serostatus using data from the ANDZATA registry. Additionally we surveyed the ANZSN and TSANZ membership to determine current clinical practice for CMV prophylaxis.

Results: Over a follow-up of 48,742 person-years, 2028/7513 recipients died. Overall, there was no significant association between CMV serostatus, all-cause and cause-specific mortality (Table 1). However, the association between CMV serostatus and cancer death was modified by human leukocyte antigen (HLA) matching (p-value for interaction < 0.001). Compared to the reference (CMV D+/R+), the adjusted hazard estimates for cancer death in those with CMV D-/R-, D-/R+ and D+/R- were 0.49 (95%CI: 0.25 – 0.95), 1.44 (95%CI: 0.98 – 2.11) and 1.04 (95%CI: 0.68 – 1.61), respectively in recipients with HLA ABDR 0–1 mismatches. Over 80% of transplanted patients who are D+ are given prophylaxis for CMV with 95% using valganciclovir. Most units use prophylaxis for 3 months, however 6 months is prescribed in D+/R- in over half of responses.

Conclusions: The association between CMV serostatus and cancer mortality appears to be modified by the number of HLA broad antigen mismatches. Use of Valganciclovir as prophylaxis is high in ANZ.

## TABLE 1.

<table>
<thead>
<tr>
<th>CMV status</th>
<th>HR 95%CI</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease related death*</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>D+/R+</td>
<td>0.85</td>
<td>0.65 – 1.11</td>
</tr>
<tr>
<td>D+/R-</td>
<td>0.99</td>
<td>0.79 – 1.26</td>
</tr>
<tr>
<td>D-/R+</td>
<td>0.94</td>
<td>0.68 – 1.29</td>
</tr>
<tr>
<td>D-/R-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection related death #</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>D+/R+</td>
<td>0.88</td>
<td>0.65 – 1.21</td>
</tr>
<tr>
<td>D+/R-</td>
<td>0.96</td>
<td>0.72 – 1.27</td>
</tr>
<tr>
<td>D-/R+</td>
<td>0.76</td>
<td>0.52 – 1.18</td>
</tr>
<tr>
<td>D-/R-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer related death**</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>D+/R+</td>
<td>1.10</td>
<td>0.91 – 1.33</td>
</tr>
<tr>
<td>D+/R-</td>
<td>1.11</td>
<td>0.92 – 1.32</td>
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<tr>
<td>D-/R+</td>
<td>1.07</td>
<td>0.85 – 1.35</td>
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<tr>
<td>D-/R-</td>
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</table>

*adjusted for age of the recipient, age of the donor, smoking status, duration on dialysis, HLA ABDR matching, year of transplantation.

# adjusted for age of the recipient, age of donor, smoking status, duration on dialysis, HLA ABDR matching, year of transplantation, prior history of cancer, cardiovascular disease, diabetes and BMI.

**adjusted for age of the recipient, age of donor, smoking status, duration on dialysis.

RENAL TRANSPLANTATION AND THE INCIDENCE OF BK AT 3 MONTHS POST TRANSPLANT

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1Renal Transplant Unit, Royal Prince Alfred Hospital, Sydney, 2Department of Renal Medicine, Sir Charles Gairdner Hospital, Perth

Background: Polyoma BK virus infection results in latency in the urothelium and can lead to viraemia and subsequent nephropathy following kidney transplantation. BK nephropathy is a significant cause of long term graft dysfunction and graft loss.

To assess the utility of testing for BK infection as part of a 3 month screening protocol.

Methods: A retrospective review of BK screening by PCR and biopsy was undertaken in 363 patients transplanted at a single centre (January 2010 - September 2015). Patients had a minimum of 3 month followup. Graft and patient outcomes were examined.

Results: 363 patients were screened. 28 (7.7%) patients had BK viremia. Of these 10 (35.7%) were low positive (<1000 copies) and a further 18 (64.3%) had intermediate or high levels. 6 patients in the latter group (33%) had BK nephropathy on biopsy being 1.7% of screened cohort.

Patients who did not have nephropathy were monitored fortnightly and where possible immunosuppression was reduced. All returned to low positive or negative in time. Patients with BK nephropathy were treated with cidofovir +/- leflunamide.

4 patients cleared the BK virus on PCR, 1 patient had ongoing low positive viraemia but no nephropathy, whilst 1 patient died due to cardiovascular complications during the treatment period with cidofovir and leflunamide.

Conclusion: Screening for BK infection routinely at 3 months resulted in detection of viraemia and nephropathy which was responsive to therapeutic intervention. Protocolised screening at this timepoint is likely to have prevented subsequent development of clinically significant BK infection.
RESULTS OF A BIOPSY BASED, EARLY INTERVENTION TREATMENT PROTOCOLS FOR BK VIREMIA AND BK VIRUS ASSOCIATED NEPHROPATHY

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1Renal Transplant Unit, John Hunter Hospital, Newcastle, 2Department of Microbiology, John Hunter Hospital, Newcastle, 3Department of Medicine, John Hunter Hospital, Newcastle

Background: This study reports our experience (January 2006 – September 2015) with early detection and intervention for BKViremia and BKVAN.

Methods: Patients detected to have BKViremia or decoy cells had transplant biopsies. Biopsies were also performed on all patients at 3 months. Those treated for BKVAN were re-biopsied after each course of treatment. Management of BKViremia involved substitution of Mycophenolate with Leflunomide, halving Tacrolimus dose and corticosteroid reduction. The BKVAN protocol required addition of Cidofovir (0.25-0.50 mg/kg IVI fortnightly x 4 doses). A second course of Cidofovir with IVIG was given for persistent BKVAN. If the biopsy was deemed to show likely acute rejection, pulsed Methylprednisolone or Thymoglobulin/PLEX/IVIG was given prior to the BK protocol.

Results: BKViremia was detected in 57/264 (21.7%), of which 37/57 (64.9%) had decoy celluria. 22/264 (38.6%) had biopsy proven BKVAN. 11/22 patients required a single course of Cidofovir; 7/22 patients completed a second course; 4 patients had an aborted course because of SAE’s (neutropenia = 4, AKI = 1). BKViremia clearance rate is shown in table 1. Creatinine/eGFR at index biopsy and 6 months later improved in 14/2 (63%), unchanged in 4/22 (16.2%) and deteriorated in 4/22 (18.2%) of patients. No grafts were deemed to be lost from BKVAN. Two grafts were subsequently lost from chronic rejection however both having cleared the virus prior. There was 1 death unrelated to BKV.

Conclusion: Biopsy based, early intervention for BKViremia and BKVAN results in viral clearance and improved graft function in the majority of affected patients.

TIME-DEPENDENT CHANGES IN CARDIAC BIOMARKERS AND CARDIAC MAGNETIC RESONANCE IMAGING (CMRI) DETERMINED CARDIAC STRUCTURE AND FUNCTION IN END-STAGE KIDNEY DISEASE (ESKD) AND FOLLOWING RENAL TRANSPLANTATION

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Background: Defining reversible and irreversible cardiac pathophysiology using cMRI and cardiac biomarkers may provide mechanistic and therapeutic insights for CKD associated cardiovascular disease (CVD).

Characterise changes in cardiac pathology by cMRI/TTE, high-sensitivity cardiac troponin T (hs-cTnT) and NT-proBNP in ESKD and following renal transplantation.

Methods: Ongoing prospective, study in incident renal transplant recipients (RTR) (n = 25, 44% preemptive, follow-up complete n = 19), prevalent haemodialysis (HD) patients (Satellite-HD, n = 26; Home-HD, n = 14). cMRI/TTE were performed at enrolment and after 12 months follow up. Serial cardiac biomarkers and routine serum biochemistry (18 timepoints) were analysed.

Results: At baseline (n = 65) no difference in any cardiac imaging parameter was observed between subgroups of ESKD. After 12 months, a significant reduction in LVMI (cMRI but not TTE) was measured for RTR (n = 19, mean (95% CI) 69 g/m² (60-77 g/m²) vs 62 g/m² (55-69 g/m²) p = 0.03) but not for HD patients (n = 22 Satellite-HD: 13 Home-HD mean (95% CI) 82 g/m² (74-90 g/m²) vs 83 g/m² (75-91 g/m²) p = 0.63). Following GFR stabilization, RTR demonstrated continued significant decline in hs-cTnT (p < 0.0013) and NT-proBNP (p < 0.0003). Furthermore, hs-cTnT but not NT-proBNP correlated strongly with LVMI at baseline (r = 0.71, p < 0.0001) and 12 months (r = 0.77, p < 0.0001) Fig 1. Significant associations with LVMI were: mean arterial pressure (p = 0.025), any CVD (p = 0.011) and logs-hs-cTnT (p < 0.001) at baseline, and any CVD (p = 0.046), logarithmic-TnT (p = 0.001) and logNT-proBNP (p = 0.01).

Conclusions: This is 1 of the largest cohort studies utilising cMRI demonstrating that LVMI reduces following kidney transplantation and hs-cTnT levels reflect this change. Ongoing analysis of cardiac fibrosis, trophic changes and global-longitudinal-strain should provide further mechanistic insights into CVD in CKD.

TABLE 1. BK Viremia clearance rate after protocol treatment

<table>
<thead>
<tr>
<th>BK Virus not detected</th>
<th>BK Virus detected below cut off</th>
<th>BK virus detected above cut off</th>
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<tr>
<td>BK Viremia: 57 Patients</td>
<td>38 (66.7%)</td>
<td>11 (19.3%)</td>
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<tr>
<td>BKVAN: 22 patients</td>
<td>15 (68.2%)</td>
<td>4 (18.2%)</td>
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FIG. 1. Correlation between high-sensitivity cardiac troponin T and LVMI measured by cMRI at baseline and 12 months.
**CARDIOVASCULAR MAGNETIC RESONANCE NONINVASIVELY DETECTS CARDIAC TRANSPLANT REJECTION: A PROSPECTIVE, HISTOLOGICALLY-VALIDATED STUDY**

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**Background:** Endomyocardial biopsies (EMBx) are required for transplant rejection surveillance but are associated with potentially serious complications. Cardiovascular Magnetic Resonance (CMR)-based tissue characterisation using T1 and T2 mapping sequences detects interstitial oedema in myocarditis. This study aimed to determine the role of CMR in the detection of cardiac transplant rejection.

**Methods:** Patients underwent CMR within 24 hours of their EMBx which was also stained with Masson’s trichrome to assess interstitial fibrosis. Serum troponin T and pro-BNP levels were also measured.

**Results:** Of 84 scans, 42 were in group 0 (ISHLT grade 0), 27 in group 1 (ISHLT grade 1R), and 15 in group 2 (ISHLT grades 2R, 3R, antibody mediated or clinically-diagnosed rejections). T1 values were significantly higher in group 2 (1033 ± 10.42; mean (SEM)) vs. group 0 (983 ± 7.18; mean (SEM)) vs. group 1 (955.2 ± 17.06; p = 0.01). T2 values were also significantly higher (in group 2 (67.59 ± 1.95) vs. group 1 (56.07 ± 2.266) and group 0 (53.60 ± 0.687; all p ≤ 0.0001). Left ventricular ejection fraction, troponin T and pro-BNP did not correlate significantly with rejection. The combination of T2- and T1-mapping data further improved transplant rejection detection (100% sensitivity, 85% specificity, and a 100% negative predictive value). Patients with more histologically-determined interstitial fibrosis also had higher T1 values (p < 0.05).

**Conclusion:** Novel CMR-based tissue characterisation displays excellent negative predictive capacity and holds promise to improve the noninvasive detection of cardiac allograft rejection.

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**ASSOCIATION BETWEEN DELAYED GRAFT FUNCTION AND LONG-TERM OUTCOMES AFTER KIDNEY TRANSPLANTATION FROM DONORS AFTER CIRCULATORY DEATH**

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**Background:** Delayed graft function (DGF) is associated with worse long-term outcomes after kidney transplantation from donation after brain death (DBD) donors. We aimed to determine whether this association held for transplantation from donation after circulatory death (DCD) donors.

**Methods:** Using data from the Australia and New Zealand Organ Donor (ANZOD) and Australia and New Zealand Dialysis and Transplant (ANZDATA) Registries, we included adult recipients of deceased donor kidney-only transplants in Australia and New Zealand over 2000–2014 (n = 6748), excluding grafts with <7 days function (n = 181). DGF was defined as the need for dialysis within 72 h of transplantation. The relationship between DGF and death-censored graft survival was examined in a Cox model adjusted for donor, transplant and recipient factors.

**Results:** DGF occurred in 22% of DBD and 55% of DCD transplants (p < 0.001). On unadjusted analysis DGF was associated with worse death-censored graft survival in both DBD and DCD donors (figure). After adjusting for confounders, the hazard ratio (HR) (95% CI) for DGF was 1.32 (1.11, 1.58) in DBD transplants and 1.77 (0.87, 3.58) in DCD transplants (interaction HR 1.34 (0.65, 2.77), p = 0.11).

**Conclusions:** DGF was associated with worse death-censored graft survival in both DBD and DCD kidney transplants, with no statistically significant difference in the magnitude of this association between DBD and DCD transplants.

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**FIGURE 1.** A. EMBx tissue with Masson’s Trichrome stain demonstrating interstitial myocardial fibrosis. 1. B. Comparison of T1 and T2 values between various rejection groups. Group 0: ISHLT grade 0, Group 1: ISHLT grade 1R, Group 2: ISHLT grades 2R, 3R, antibody mediated or clinically-diagnosed rejection and clinically-diagnosed rejection. 1. C. ROC curves for T1 and T2 values measured along the interventricular septum (septal T1 & T2) as well as circumferentially at mid-ventricular short axis slice (Global T1 and T2) to diagnose rejection in heart transplant recipients. The area under the curve for combined T1 and T2 values was 0.946 with sensitivity of 100% and specificity of 85%.
SHORT TERM SURGICAL COMPLICATION RATES IN TRANSPLANT SURGERY: CONSULTANT VS TRAINEE

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Background: To investigate whether there is a significant difference between the short term surgical complication rates when either the Consultant or the Trainee is the primary surgeon for transplant operations.

Method: All patients who had a cadaveric, live renal or simultaneous pancreas kidney (SPK) transplant at Westmead Hospital from August 2014 – August 2015 were included. Data was collected on patient demographics, primary surgeon and surgical complications. Short term surgical complication was defined as a complication that occurred within 30 days of surgery. Complications were graded using Clavien-Dindo classification and also grouped into types of complication.

Results: There were 101 patients in this study (21 live, 53 cadaveric renal transplants and 27 SPK). There were 55 complications in 46 patients with bleeding as the predominant complication. The majority of complications were in the Clavien-Dindo Grade III group (requiring surgical or radiological intervention). The SPK complication rate for the Consultant was 75% compared with 66.7% (P = 0.64) for the Trainee. The live renal transplant complication rate for the Consultant was 41.2% compared with 25% (P = 0.55) for the Trainee. The cadaveric renal transplant complication rate for the Consultant was 64% compared with 39.3% (P = 0.07) for the Trainee.

Conclusion: This study found that there is no significant difference between the short term surgical complication rates when either the Consultant or Trainee was the primary surgeon for all 3 transplant operations. However, the Consultant compared to the Trainee had the higher complication rate for all transplant operations. This result may reflect that Consultants typically operated on the more complex cases.

FIGURE 1.

Overall graft survival
Aust/NZ adult deceased donor kidney transplants 2000-2014

| DCD DGF- | 381 | 309 | 258 | 193 | 133 | 75 |
| DCD DGF+ | 453 | 354 | 268 | 192 | 121 | 77 |
| DBD DGF- | 4485 | 4003 | 3677 | 3136 | 2756 | 2379 |
| DBD DGF+ | 1258 | 1044 | 876 | 748 | 646 | 553 |

Years post transplant
NEPHROGENIC ADENOMA - A CASE REPORT AND UPDATE

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Background: Nephrogenic adenoma (NA) is a benign adenomatous lesion of the urinary tract. Long considered a rare phenomenon, case series from the renal transplant population suggest that it may be much less uncommon within this group. The pathogenesis of NA remains to be clearly elucidated, however recent studies support the hypothesis that NA represents the proliferation of renal tubule cells that have been shed, and reimplanted within the lower urinary tract. While NA is considered a lesion with low premalignant potential; haematuria, lower urinary tract symptoms and recurrent urinary tract infections are frequently observed in the context of NA. Furthermore, following resection of NA, lesion recurrence and persistent symptoms frequently remain problematic.

Methods: Here we present the case of a 69-year-old male renal transplant recipient with NA, and a review of the literature.

Results: Our patient’s clinical course was characterised by recurrent urinary tract infection with associated graft dysfunction, despite cystoscopic resection of the primary lesion.

Conclusions: This case is illustrative of the clinical impact of NA, and the need for ongoing work into the development of strategies to manage this problematic phenomenon.

SCLEROSING PERITONITIS FOLLOWING LIVER TRANSPLANTATION: A CASE SERIES

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Background: Sclerosing peritonitis (SP) is a rare but potentially fatal complication following liver transplantation. It has been linked to refractory ascites, biliary obstruction, IVC and porta hepatitis obstruction. The definitive surgical management is via laparotomy and PEEL procedure, but carries risks particularly in the immunosuppressed transplant patient population. The natural history of SP is known from a handful of case reports and series, which report de novo cases arising early in the weeks.

To identify the incidence of SP following orthotopic liver transplantation (OLT) and the outcomes post management.

Methods: 2 cases of late development of SP post OLT were identified from the Australian National Liver Transplantation Unit database.

Results: 2 cases of SP were identified, 1 diagnosed at 2 years and the other at almost 10 years post transplantation. Both patients presented with symptoms suggestive of small bowel obstruction. CT scan of the abdomen of patient 1 was suggestive of an internal hernia and patient 2 showed a transition point in the distal jejunum. After failing conservative measures, both patients proceeded to laparotomy and a PEEL procedure was undertaken of the cocooned bowel.

Conclusions: SP should be considered as a differential diagnosis in patients post OLT presenting with symptoms of bowel obstruction, even years after the transplantation.
CIRCULATING DNA: AN APPROACH TO MONITOR ORGAN REJECTION AFTER LIVER TRANSPLANTATION

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Background: Up to twenty percent of patients will develop an episode of rejection in the first twelve months after liver transplantation. Liver biopsy is the gold standard for the diagnosis of organ rejection. However, this procedure is invasive and carries a risk of bleeding and sepsis. Recent studies have proposed the use of donor-specific circulating cell-free DNA (dscfDNA) as a blood-based biomarker for organ rejection. Unlike current methodologies used to quantify dscfDNA, we aimed to develop a rapid and cost-effective approach for serial monitoring of graft health after liver transplantation.

Methods: Five patients undergoing liver transplantation were prospectively recruited. Droplet digital PCR was used to analyze recipient blood samples collected at various timepoints. This PCR platform allows precise quantification of dscfDNA molecules in the circulation of the recipient. The levels of dscfDNA were compared with serum liver biochemistry and clinicopathological factors.

Results: Levels of dscfDNA were reflective of graft health. Marked increase in dscfDNA levels were observed in 1 patient who developed an episode of acute cellular rejection. Cholestasis did not increase the levels of dscfDNA after liver transplantation. Turnaround time for quantification of dscfDNA is attainable under 6 hours.

Conclusion: Our methodology to accurately quantify dscfDNA was feasible and clinically applicable. Furthermore, our preliminary results suggest that this noninvasive biomarker can facilitate timely and serial monitoring of graft health for organ rejection.

CELL-FREE DNA CAN IDENTIFY MILD CELL MEDIATED REJECTION IN PAEDIATRIC HEART TRANSPLANT RECIPIENTS

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Background: To measure graft-derived cell-free DNA (gdcfDNA) and total cfDNA (tcfDNA) in paediatric heart transplant recipients (PHTR) as proof of principle application of our digital droplet PCR (ddPCR) methodology based upon ubiquitous copy number variation (CNV) differences between donor and recipient.

Methods: Cf-DNA was extracted from plasma collected longitudinally from 13 PHTR. A panel of ddPCR assays directed at polymorphic CNV loci was used to absolutely quantify gdcfDNA and tcfDNA. Variation in cfDNA levels over time was correlated with protocol biopsy results.

Results: In all recipients, gdcfDNA and tcfDNA was detected and quantified. There were a total of 17 rejection episodes (16x grade 1 cell mediated rejection (CMR) and 1x grade 2 CMR). The combined interpretation of gdcfDNA, tcfDNA and graft fraction was able to identify CMR (by rising above baseline levels before or on the day of biopsy) in 9/17 occasions. In 5/8 false negatives, there was insufficient sampling, no preceding normal biopsy or excessive variation that prevented establishment of a baseline level. Establishment of a diagnostic threshold was difficult given variation in observed baseline levels. In a further 2/8 false negatives, the failed identification of rejection occurred after successful identification of an earlier episode.

Conclusion: GdcfDNA can be quantified in PHTR using our methodology. Given other genomic diagnostic methods have performed poorly in paediatric recipients and detection of mild CMR, our method warrants further investigation. More frequent sampling and correction for body size/weight may improve diagnostic performance.
PYELOURETERIC JUNCTION OBSTRUCTION OF RENAL ALLOGRAFTS
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Background: Congenital Pyeloureteric Junction (PUJ) obstruction is present in 1/500 live births. Baggy extra renal pelvises are more frequently encountered. PUJ obstruction in kidney transplantation is uncommon problem and literature is sparse. Following transplantation the obstruction may become urodynamically significant due to diuresis, autonomic denervation, minor ureteric torsion, kink, external scarring or reduced blood supply.

Methods: We report 2 cases of PUJ obstruction in renal allograft recipients.

Results: In the first case, following deceased donor transplant, PUJ obstruction was diagnosed following stent removal. In the second case a 5 mm stone was noted in baggy extra renal pelvis during live donor assessment. Back table flexible ureteroscopy was planned with standard CH6 instrument. During the procedure the ureteroscope could not be advanced through the PUJ.

Conclusions: Options for reconstruction of transplant PUJ obstruction include native ureteropyelostomy, Boari flap vesicopyelostomy, nondismembered flap reconstruction, long term stenting or nephrostomy. Both of our cases were reconstructed with native ureteropyelostomy with good intermediate term outcomes.

Xenotransplantation & Cells/Tissues-Experimental
GTKO/CD55-CD59-HT PORCINE NEONATAL ISLET CELL CLUSTER (NICC) XENOGRAFTS PROVIDE LONG-TERM REVERSAL OF DIABETES
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Background: Transgenic expression of human complement regulatory proteins or deletion of αGal (GTKO) has been shown to protect porcine islet xenografts in monkeys treated with costimulation blockade-based immunosuppression. However, this has not been examined in the immunologically more challenging baboon model. We investigated the combined effects of these modifications on the outcome of intraportal NICC transplantation in immunosuppressed baboons.

Methods: 1–5 day old GTKO piglets transgenic for human CD55, CD59 and H-transferase were used as donors. Recipient baboons received GTKO/CD55-CD59-HT NICC under standard (ATG, tacrolimus, mycophenolate mofetil; n = 5) or costimulation blockade-based immunosuppression (anti-CD2, anti-CD154, belatacept, tacrolimus; n = 4). Graft survival and function was followed by daily blood sugar levels, IVGTT and graft immunohistochemical analysis for up to 12 months posttransplant.

Results: GTKO/CD55-CD59-HT xenografts exhibited no signs of early thrombosis or infiltrate, nor changes to recipient platelet counts, fibrinogen and D-dimer levels from baseline. However, liver biopsies from recipients under standard immunosuppression revealed rejection of NICC within one month. Changing to costimulation blockade-based immunosuppression reduced cellular infiltration, and cells staining positive for insulin, glucagon and somatostatin were present in all xenografts at 3 months. On the extended protocol the 2 animals performed thus far have normal glucose handling out to as far as one-year post transplant.

Conclusions: Deletion of αGal and expression of human CD55 and CD59 prevent early thrombotic destruction of porcine NICCs in the baboon model. Costimulation blockade-based immunosuppression appears to be more effective than standard immunosuppression in prolonging the survival of genetically modified porcine NICC xenografts.
PROTECTION FROM INSTANT BLOOD MEDIATED INFLAMMATORY REACTION IN GAL-KO PORCINE NEONATAL ISLET CELLS EXPRESSING COMPLEMENT REGULATORS CD55/CD59

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Background: Clinical islet cell transplantation is a viable treatment option for type-1 diabetes. Unfortunately the lack of donor pancreata remains a major hurdle to offering this treatment to larger groups of patients. Porcine Neonatal Islet Cell Clusters (NICC) are a suitable alternative to human islets. However, hyperacute rejection (HAR) and the Instant Blood Mediated Inflammatory Reaction (IBMIR) pose major problems following NICC transplantation.

To explore the benefits of using galactosyltransferase knock-out (gal-KO) or gal-KO NICC expressing the complement regulators CD55/CD59 transgene (gal-KO CD55/59-tg), on xenogenic IBMIR in vitro.

Methods: IBMIR was compartmentalised in vitro, to measure independently, the effect of thrombosis, complement and neutrophil activation on wild-type vs. transgenic NICC.

Results: The peak thrombin concentration and thrombin time were similarly elevated between gal-KO (198.3 ± 83.1 nM; 15.0 ± 4.4 minutes) and wild-type NICC (188.6 ± 29.3 nM; 16.2 ± 3.9 minutes), but the combination of gal-KO CD55/59-tg NICC provided significantly delayed thrombin generation (23.9 ± 6.2 minutes, P < 0.05) and reduced peak thrombin levels (69.9 ± 27.7 nM, P < 0.05). Formation of complement C3a was significantly reduced when gal-KO (76.9 ± 3.6 ng/mL) or gal-KO CD55/59-tg (67.1 ± 9.5 ng/mL) NICC was exposed to human blood compared to WT NICC (542.7 ± 334.5 ng/mL; P < 0.05). Furthermore, significant reduction in neutrophil activation was observed in both gal-KO and gal-KO CD55/59-tg NICC compared to WT NICC (WT: 1.7 ± 0.2-fold, gal-KO: 0.89 ± 0.1-fold or gal-KO CD55/59: 1.1 ± 0.02-fold, P < 0.05).

Conclusions: Our data demonstrated that whilst removing the galactosyltransferase gene partially protected NICC against IBMIR, additional regulators such as the complement inhibitors CD55 and/or CD59 is critical to ensure successful NICC transplantation.

IL-28 IS A CRITICAL CYTOPROTECTANT IN TRANSPLANTATION

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Background: We have demonstrated a protective role for type I Interferons (IFN) through inhibition of Th1 differentiation invoked by recipient CD8neg dendritic cells after experimental bone marrow transplantation. Recently described Type III IFNs (IFNλ/IL-28) signal through the unique IL-28R primarily expressed in epithelial tissues and implicated in mucosal pathogen defence. Clinical use of type I IFN is associated with adverse neurological, haematological and constitutional symptoms where IL-28 is better tolerated, yet still demonstrates potent anti-viral effects.

Methods: We used IL-28R +/- and IFNaR1+ donors and recipients in murine models of GVHD and GVL to develop logical therapeutic strategies to improve transplant outcomes.

Results: IL-28R +/- donors invoked similar GVHD and GVL to WT. However IL-28R +/- recipients had accelerated acute GVHD (aGVHD) mortality and disease relative to WT with a phenotype intermediate to that and the hyperacute aGVHD seen in IFNaR1+ recipients (median survival WT 42 vs. IL28R +/- 26 vs. IFNαR1+ 6.5 days, p=<0.0001). IL28R +/- recipients have augmented colonic GVHD histopathology early (d 7) after BMT (WT 7.111±0.6550 vs. IL28R +/-12.33±0.7993, p=0.0004) and exaggerated inflammatory cytokine generation (d4 IFNα WT 331±41.47pg/mL vs. IL28R +/-667±48.79 pg/mL, p=<0.0001 and IL-6 WT 61.25±10.91 pg/mL vs.IL28R +/- 91.99±11.23pg/mL, p=0.024). Re-transplantation of chimeras with WT or IL28R +/- haematopoietic, nonhaematopoietic tissue or combinations thereof demonstrated that IL-28 mediated protection required signalling through both compartments, putatively recipient antigen presenting cells and colonic epithelia.

Conclusion: IL-28 represents an attractive therapeutic to mediate cytoprotection within the GI tract and attenuate to GVHD in the peri-transplant period.
TRANSGENIC EXPRESSION OF HUMAN THROMBOMODULIN INHIBITS HMGB1-INDUCED PIG AORTIC ENDOTHELIAL CELL ACTIVATION

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Background: Transgenic expression of human thrombomodulin (hTBM), a species-specific vascular anti-coagulant, has the potential to solve the problem of coagulation dysregulation in pig-to-primate xenotransplantation. However, the further benefits of hTBM via its anti-inflammatory properties, notably against the proinflammatory cytokine high-mobility group box 1 (HMGB1), have not been examined.

Aim: To test HMGB1-mediated effects on wild-type (WT) porcine aortic endothelial cells (PAEC), and to assess the capacity of hTBM on PAEC to neutralize HMGB1.

Methods: WT and hTBM-transgenic PAEC were treated with HMGB1, hTNFα or lipopolysaccharide (LPS) and analysed for expression of cell surface markers, secretion of porcine cytokines and chemokines, and formation of tPA/PAI-1 complexes. Thrombin-induced HMGB1 cleavage in the presence of PAEC was examined by western blot and functional assays.

Results: HMGB1 potently activated WT PAEC, increasing the surface expression of E-selectin, VCAM-1, ICAM-1, FGL2 and PAI-1, and the secretion of TNFα, IL-8, and MCP-1. hTNFα- or LPS-induced activation of WT PAEC was inhibited by treatment with rabbit anti-HMGB1 antibody. Transgenic hTBM significantly attenuated HMGB1- or hTNFα-induced PAEC activation, and significantly enhanced thrombin-mediated HMGB1 cleavage. Removal of the lectin-like domain of TBM resulted in significantly increased HMGB1- or hTNFα-induced PAEC activation.

Conclusion: HMGB1 stimulated powerful proinflammatory and procoagulant effects on WT PAEC. Transgenic hTBM, via its lectin-like domain, significantly inhibited HMGB1-mediated actions on PAEC and increased thrombin-induced degradation of HMGB1 to a less proinflammatory form. These results indicate that transgenic hTBM has anti-coagulant and anti-inflammatory effects that are likely to be beneficial in pig-to-primate xenotransplantation.

CONJUGATION OF APYRASE TO PORCINE AORTIC ENDOTHELIAL CELLS PROLONGS CLOTTING OF WHOLE HUMAN BLOOD

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Background: Recipient platelets play an important role in the dysregulated coagulation that is frequently observed in pig-to-primate xenotransplantation. ADP is essential for activation of platelets and coagulation, and is an obvious target for platelet inhibition.

To investigate the impact of surface immobilization of the ATP/ADP-degrading enzyme apyrase on porcine aortic endothelial cells (PAEC) in xenotransplantation-induced thrombosis. Methods: PEG-conjugated phospholipid was used to immobilize apyrase on the PAEC surface. The enzymatic activity of apyrase-PAEC was evaluated as ATPDase activity. The anti-coagulant properties of apyrase-PAEC were tested using a microcarrier bead-based coagulation assay with freshly drawn nonanticoagulated whole human blood in a proportion that closely mimics the in vivo small vessel endothelial surface-to-blood volume ratio.

Results: Immobilization of Alexa 488-labeled apyrase on PAEC was confirmed by immunofluorescence/confocal microscopy. Beads coated with apyrase-PAEC degraded exogenously added ATP in a dose-dependent manner (ATPDase activity: 9.9±1.1 nmol/20min at 10μg/ml apyrase; 17.7±0.6 at 25μg/ml). Immobilized apyrase retained approximately 81% of the activity of the native form. Apyrase-PAEC significantly prolonged clotting of human blood (70.4±17.7 min, p<0.001 vs. untreated PAEC: 32.5±6.9 min). The concentration of markers of complement activation (sC5b-9) (p=0.015), coagulation activation (thrombin-antithrombin complex and D-dimer) (both, p<0.0001) and inhibition of fibrinolysis (tPA/PAI-1) (p<0.0001) was lower in EDTA-plasma of coagulation assays with apyrase-PAEC than untreated PAEC.

Conclusion: Apyrase-immobilized PAEC inhibit xenogenic platelet activation and suppress coagulation in a whole blood assay. This assay can be used to evaluate the potential of novel therapeutic substances not only in xenotransplantation but also in allotransplantation and ischemia/reperfusion injury.
A NEW PORCINE MODEL OF NORMOTHERMIC MACHINE PERFUSION OF LIVER DONATION AFTER CIRCULATORY DEATH: A PRELIMINARY STUDY

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Background: Interventions aimed at improving liver donations after circulatory death (DCD) are under active investigation on account of poor outcomes of human DCD liver recipients. However, current large animal models induce circulatory death by either exsanguination or potassium chloride injection, neither of which are practised clinically. We sought to develop a clinically relevant model of DCD liver retrieval followed by normothermic machine perfusion (NMP).

Methods: Landrace pigs (60-70 kg) were anaesthetised and intubated. To mimic clinical practice, cessation of mechanical ventilation was used to induce circulatory death, which was confirmed by ECG electrical silence or disappearance of pulse pressure. A 5 min stand-off period was instituted prior to cold preservation flush of the liver and explantation. The liver was subsequently prepared on the backtable for machine perfusion.

Results: 12 donor animals underwent this protocol. Average time to asystole was 9.27 min. Average warm ischaemic time, as defined from ventilation cessation to cold preservation flush, was 20.25 min. Livers were maintained on machine perfusion for 4 hours, exhibiting favourable aminotransferase release, lactate and pH profiles and bile production.

Conclusions: Further research is required to identify optimal time of NMP and potentially optimise liver preservation with improved perfusion parameters and pharmacological reconditioning agents in perfusate.

FIGURE 1. Successfully machine perfused porcine liver

MICROARRAY GENE PROFILING OF IMMUNOSUPPRESSIVE INTERLEUKIN-17A PREACTIVATED HUMAN BONE MARROW-DERIVED MESENCHYMAL STEM CELLS (MSC-17)

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Background: MSC-17 are superior T cell immunomodulators for clinical allotransplantation.

Methods: Untreated-MSC (UT-MSC) or 5-days IFN-γ (MSC-γ) or IL-17A (MSC-17) treated MSC were assessed for T cell immunosuppression and ability to induce Tregs. Immunophenotype (flow cytometry) and gene expression profile (microarray) of 3 MSC donors were also analyzed. Significantly regulated genes (p<0.05, fold change (FC)<-2 or >2) were identified for their biological functions (Database for Annotation, Visualisation and Integrated Discovery, DAVID).

Results: MSC-17 potently suppressed PHA-induced T cell proliferation (3H-thymidine) and T cell activation (downregulated CD25, IFN-γ, TNF-α, IL-2) by inducing Tregs expressing functional Treg markers (CD39, CD73, CD69, OX40, CTLA-4, GITR). Different to MSC-γ, MSC-17 showed no upregulation of MHC or CD40 molecules. Microarray analyses identified 1278 differentially regulated genes (902 upregulated; 376 downregulated) between MSC-γ and UT-MSC; and 67 genes (39 upregulated; 28 downregulated) between MSC-17 and UT-MSC. MSC-γ were enriched for genes involved in immune response, antigen processing and presentation, humoral response and complement activation; consistent with increased MSC-γ immunogenicity. MSC-17 genes were associated with chemotaxis response, which may be involved in T cell recruitment for MSC-17 immunosuppression. MSC are known to express MMP with chemotaxis and immunosuppressive properties. MMP13 was highly expressed specifically in MSC-17 (FC 15.6) and was validated by RT-PCR. Hence, MMP13 may mediate the superior immunomodulatory function of MSC-17.

Conclusion: MSC-17 represent a potential cellular therapy to suppress immunological T cell responses in allotransplantation, with minimal immunogenicity. Studies on the functional role of the key candidate molecule MMP13 in MSC-17 immunomodulation are currently underway.
Ischaemia Reperfusion Injury, Metabolism and Islet Transplantation

MATRICELLULAR ACTIVATION OF CD47 LIMITS SELF-RENEWAL TO PROMOTE RENAL ISCHEMIA REPERFUSION INJURY

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Background: Ischemia reperfusion injury (IRI) is a consequence of transplantation and initiates kidney repair. The basis for maladaptive repair following IRI remains unclear, although preclinical studies have verified a defect in renal tubular epithelial cell (rTEC) proliferation. We reported that the matricellular protein thrombospondin-1 (TSP1), and its receptor CD47 are induced in renal IRI, although their role in recovery is unknown.

Methods: Age-matched wild-type (WT) and CD47-/- mice were challenged with bilateral renal IRI. WT mice underwent syngeneic renal transplant with some recipients treated with CD47 blocking antibody. All animals underwent assessment of renal function and biomolecular analysis. Human and murine rTEC were studied in vitro.

Results: Mice lacking CD47 were resistant to renal IRI with decreased urea and creatinine, and demonstrated return of renal function after 7 days, compared to ongoing renal impairment in WT controls. CD47-/- animals displayed constitutive upregulation of self-renewal genes cMyc, Klf4, Oct4, and Sox2. WT animals demonstrated negligible self-renewal gene expression at all time points. Following kidney transplantation, administration of a CD47 blocking antibody to the recipient improved serum creatinine and upregulated self-renewal targets. Indicative of a cell-dependent process, CD47-/- rTEC displayed basal upregulation of self-renewal genes that correlated with enhanced proliferative capacity. Addition of TSP1 to WT rTEC downregulated self-renewal gene expression, which was not seen in CD47-/- cells. Conversely, treatment with a CD47 antagonist antibody increased self-renewal and promoted proliferation.

Conclusions: CD47 impairs rTEC recovery through inhibition of self-renewal, and thus may be a possible clinical target to facilitate organ repair following transplantation.

SIGNAL INHIBITORY REGULATORY PROTEIN-α#913; REGULATES GENERATION OF PATHOLOGIC REACTIVE OXYGEN SPECIES IN ACUTE KIDNEY INJURY

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Background: Ischemia reperfusion injury (IRI) is mediated by reactive oxygen species (ROS). We have recently reported that signal regulatory inhibitory protein (SIRP)-α is expressed by renal tubular epithelial cells (rTEC). We have also shown that the protein thrombospondin-1 (TSP1) is increased following renal IRI and binds to SIRPα. However, it is unclear how the TSP1-SIRPα signaling contributes to the pathophysiology of IRI.

Methods: Age-matched male wild-type (WT) mice, and SIRPα mutant (SIRPαmut) mice, which lack the cytoplasmic recruitment domains, underwent bilateral renal IRI. Animals underwent biomolecular analysis at 24h reperfusion. WT and SIRPαmut rTEC were studied in vitro. Mice were also lethally irradiated and rescued with WT or SIRPαmut bone marrow, to interrogate the contribution of the parenchymal cell compartment to IRI.

Results: IRI significantly elevated serum creatinine in WT mice, which was mitigated in SIRPαmut animals (2.3±0.46 versus 0.98±0.41 mg/dl, p<0.01). TSP1 was expressed to a similar degree post-IRI. Measurement of ROS in whole kidney demonstrated a 2-fold increase in WT mice post-IRI, but no increase in SIRPαmut or sham-operated animals. Expression of oxidative protein modification was reduced in SIRPαmut kidneys compared to WT, although expression of NADPH oxidases was unchanged. WT rTEC displayed upregulation of ROS in response to TSP1, which was not demonstrated in SIRPαmut cells. In chimeric animals, SIRPαmut mice, regardless of hematopoietic reconstitution, were protected against renal dysfunction and ROS generation following IRI.

Conclusion: These data provide genetic evidence for a role for SIRPα promoting renal IRI through generation of pathologic ROS. Blockade of SIRPα may provide a novel therapeutic target to modify IR-mediated damage.
FACTORS EFFECTING ISLET ISOLATION OUTCOMES OVER THE PAST 15 YEARS FOR THE WESTMEAD ISLET TRANSPLANT PROGRAM

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Background: Islet cell transplantation for type 1 diabetes relies heavily on successful isolation outcomes to ensure successful transplantation. As such we aimed to evaluate our islet isolation outcomes and identify factors during donor selection, organ procurement and islet isolation influencing the preparation leading to a transplant.

Methods: Islets were isolated from pancreata of heart beating deceased donors using collagenase and NP (SERVA). Donor characteristics, pancreas procurement data, isolation yield and outcomes were collected and compared to determine correlation between each variable. Isolations were also divided into Transplanted (Tx) VS Nontransplanted preparations (Non-Tx) to identify variables significantly influencing isolation outcomes.

Results: Data from 207 islet isolations collected between July 2000 and December 2015 were evaluated. On average, 24.9% of islet preparations were transplanted, with 45.8% of isolations in 2014-2015 reaching release criteria. Transplantable yields (defined as 300,000 IEQ; 4,000 IEQ/kg for a 75kg recipient) were obtained from donors aged between 20-60 years, with BMI >20kg/m², and weight >55kg. Digestion times >25 mins were found to negatively affect cell viability and yield. Compared to non-tx (n=158), Tx (n=49) had significantly higher total IEQ (611,212±329,905 VS 329,905±202,249 IEQ) and IEQ/g pancreas (8,389±6,525 VS 5,229±3,792 IEQ/g). Higher donor BMI, donor weight, pancreas weight, and lower CIT, were significantly correlated (p<0.05) to Tx. Tx also exhibited significantly higher viability, purity and beta cell viability indices compared to Non-tx.

Conclusions: We found that increased donor BMI/weight and lower CIT all have significant effects on outcomes. In particular these influence which islet isolations resulted in transplantable yields/outcomes.

POSTCONDITIONING WITH CYCLOSPORINE: IMPACT ON ISCHEMIA REPERFUSION INJURY IN A RODENT MODEL OF DONOR HEART PRESERVATION

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Background: To investigate the potential benefits of the mitochondrial permeability transition pore inhibitor cyclosporine (CsA) in donor heart preservation after 6 hours of hypothermic storage.

Methods: Isolated working rat hearts were stored for 6 hours in Celsior or St Thomas solution (STH). CsA was added to the preservation solution (0.2 or 2.0 μM) during cardioplegia and storage (2-3°C), or to KH buffer (0.2 μM) during the first 15 min or the whole 45 min of normothermic reperfusion after storage. Preservation of cardiac function was calculated by recovery of cardiac output (CO) as percentage of prestorage baseline. Lactate dehydrogenase (LDH) release during perfusion of the heart was assessed prior to and after storage.

Results: Data from 207 islet isolations collected between July 2000 and December 2015 were evaluated. On average, 24.9% of islet preparations were transplanted, with 45.8% of isolations in 2014-2015 reaching release criteria. Transplantable yields (defined as 300,000 IEQ; 4,000 IEQ/kg for a 75kg recipient) were obtained from donors aged between 20-60 years, with BMI >20kg/m², and weight >55kg. Digestion times >25 mins were found to negatively affect cell viability and yield. Compared to non-tx (n=158), Tx (n=49) had significantly higher total IEQ (611,212±329,905 VS 329,905±202,249 IEQ) and IEQ/g pancreas (8,389±6,525 VS 5,229±3,792 IEQ/g). Higher donor BMI, donor weight, pancreas weight, and lower CIT, were significantly correlated (p<0.05) to Tx. Tx also exhibited significantly higher viability, purity and beta cell viability indices compared to Non-tx.

Conclusions: We found that increased donor BMI/weight and lower CIT all have significant effects on outcomes. In particular these influence which islet isolations resulted in transplantable yields/outcomes.

CONCLUSIONS: The addition of CsA to preservation solutions during cold storage provided no additive protection. CsA improved post-storge cardiac functional recovery only when delivered for the first 15 minutes of reperfusion. Prolonged exposure to CsA during reperfusion resulted in significantly increased LDH release, suggesting direct toxicity to cardiomyocytes.
From Disease to Donation to the Final Destination – Where is Your Patient on the Transplant Journey?

A NOVEL CARDIAC ALLOCATION SCORE FOR PREDICTING WAITLIST AND POSTTRANSPLANT SURVIVAL

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Background: We propose that a survival-benefit allocation scheme similar to the lung allocation score should be considered to increase the utility of each heart donated. In this study, a novel cardiac allocation score (CAS) algorithm was developed that identifies the patient on the waiting list with the greatest expected survival benefit from transplantation.

Methods: All adult patients from the cardiac transplant waiting list at our institution, between 2008 and 2015 were included in the study (n = 260). Univariate survival analysis of prelisting variables was undertaken to ascertain factors that significantly predicted 1-year mortality on the waiting list and posttransplant. Significant variables were placed in a multivariate Cox Regression to develop models predicting pre and posttransplant survival of wait-list patients. The difference in estimated pre and posttransplant survival time gave the predicted survival benefit of transplantation; this measure was normalised, and a score between 0 and 100 was given to each patient, a higher score correlating with a higher expected posttransplant survival benefit.

Results: Two statistically significant models were developed to predict waiting list mortality (P<0.0001) and posttransplant mortality (P=0.0106) respectively. A higher CAS was shown to significantly predict higher risk for wait list mortality (HR: 1.110738, P<0.001) and lower risk for posttransplant mortality (HR: 0.8715659, P<0.001).

Conclusion: We present a novel allocation system for donor hearts that considers the expected waiting list and posttransplant survival. The clinical adoption of such a model could allow better transplant prioritisation and achieve improved outcomes for recipients postorthotopic heart transplantation.

EVALUATION OF A TRANSITION PROGRAM FOR ADOLESCENTS WITH SEVERE LIVER DISEASE/LIVER TRANSPLANT

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Background: Failure of adequate transition from paediatric to adult care results in morbidity, graft loss and mortality in liver transplant recipients.

Aims: We aimed to assess the effect of a formalised transition program using a standardised healthcare skills checklist (HSC).

Methods: Adolescents >15 years with severe liver disease/liver transplant completed a standardised HSC. They and their parents underwent a formal transition clinic program involving a transition manager, transition coordinator and youth mentor. Competencies and gaps were identified and individual goals developed. After 2 or more transition clinic visits and prior to transfer, the HSC was administered again.

Results: Of 32 adolescents who completed the program with a median of 2.3 visits, a significant improvement was seen across the following domains: Knowledge of condition (43% to 80%), knowledge of medications (50% to 80%), adherence to treatment (52% to 74%), confidence in speaking about their liver disease (30 to 71%) and independence with healthcare (16% to 55%). Anxiety regarding transfer was significantly reduced (82 to 29%).

Conclusions: A formalised transition program appears to significantly improve patient readiness for transition. We are currently assessing whether this improved knowledge is retained after the transfer process, and whether it translates to improved patient outcomes.
RESEARCH PRIORITY SETTING IN ORGAN TRANSPLANTATION: A SYSTEMATIC REVIEW
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Background: We aimed to evaluate approaches to research priority setting in solid organ transplantation and to describe the research priorities of patients, their caregivers, healthcare providers, and policy makers.

Methods: Electronic databases were searched to December 2015. Studies that elicited patient, caregiver, healthcare provider, or policy maker priorities for research in solid organ transplantation were included.

Results: We identified 16 studies (n=1250 participants) conducted in the United States, the Netherlands, Australia and Canada. The studies focused on kidney (8 [50%] studies), heart (2 [13%] studies), lung (1 [6%] study), and nonspecified solid organ transplantation (5 [31%] studies). Various priority setting methods were used including the Delphi technique, expert panels, consensus conference, ranking or voting surveys, focus groups and interviews, of which the process was described in detail by 10 (63%) studies. Only six (38%) studies reported patient involvement. The priority areas for research were: improving immunosuppression (12 [75%] studies), organ donation and allocation (9 [56%] studies), psychosocial support including adherence (8 [50%] studies), patient communication and education (7 [44%] studies), organ preservation (2 [13%] studies), wait-listing (1 [6%] study), and prevention of diabetes (1 [6%] study).

Conclusion: The research priorities identified in solid organ transplantation are broad in scope. However, few priority setting initiatives engage patients and just over half have a well-described process. Setting research priorities in an explicit manner with equitable involvement of patients can help to ensure that resources are directed towards research that is important and relevant to patients and health professionals in solid organ transplantation.

COGNITIVE AND ACADEMIC OUTCOMES IN CHILDREN WITH CHRONIC KIDNEY DISEASE AND KIDNEY TRANSPLANTS
ZWIETEN Anita VAN1,2, Kerry CHEN1,2, Madeleine DIDSBURY1,2, Jennifer LORENZO4,5, Belinda BARTON4,5, Suncica LAH6, Jonathan CRAIG1,7,2, Allison TONG1,2, Kirsten HOWARD2, and Germaine WONG1,8,2
1Centre for Kidney Research, The Children’s Hospital at Westmead, Sydney, 2School of Public Health, University of Sydney, 3Institute for Neuroscience and Muscle Research, The Children’s Hospital at Westmead, Sydney, 4Children’s Hospital Education Research Institute, The Children’s Hospital at Westmead, Sydney, 5School of Medicine, University of Sydney, 6School of Psychology, University of Sydney, 7Department of Paediatric Nephrology, The Children’s Hospital at Westmead, Sydney, 8Department of Nephrology, Westmead Hospital, Sydney

Background: Whilst chronic kidney disease (CKD) is known to reduce children’s life expectancy and physical health, disease-related biological and psychosocial factors may also impair cognitive and academic development. We aimed to examine cognitive and academic functioning in children with predialysis CKD and kidney transplants, and determine whether specific domains of cognition are differentially affected by CKD.

Methods: Tests of cognitive (IQ, attention, memory) and academic (literacy and mathematical) skills were administered to 16 children with CKD (predialysis n = 9, transplant n = 7). Their scores were classified as average (≥90 scaled score, ≥8 subtest score) or below average, and the groups were compared using independent samples t-tests.

Results: The mean age was 11.4 (SD=1.9) years, and 11 (69%) were male. On average children missed 1.7 (SD=2.5) days of school per month. The mean full-scale IQ (95.2, SD=16.96), reading (99.8; SD=15.75), spelling (94.7; SD=15.14) and mathematical skills (90.3; SD=22.37) fell in the average range. Mean scores on verbal learning/memory (6.3, SD=3.21), sustained auditory attention (7.3, SD=3.62) and divided attention (6.9, SD=2.75) were below average. Across tests no differences were found between predialysis and transplanted children (all p>0.1).

Conclusions: Children with CKD appear to have average overall intelligence and academic skills, but may experience difficulties with attention and verbal learning. Such difficulties can negatively impact daily functioning, and in turn affect overall well-being. Further research should elucidate the nature of specific cognitive deficits in children with CKD to enable the development of targeted interventions that facilitate healthy cognitive development.
INPATIENT REHABILITATION OF HEART AND LUNG TRANSPLANT PATIENTS A PHYSIOTHERAPY PERSPECTIVE- RETROSPECTIVE ANALYSIS 2011-2015 ST VINCENT’S HOSPITAL, SYDNEY

Genevieve WOODBRIDGE
Rehabilitation Medicine- Physiotherapy, St Vincent’s Hospital, Sydney

Background: To do a retrospective analysis of physiotherapy outcomes of patients admitted for inpatient rehabilitation at Sacred Heart Rehabilitation, St Vincent’s Hospital Sydney following heart, lung or heart and lung transplantation from 2011- 2015 and analysis of results and physiotherapy intervention.

Methods: A sample size of 67 patients were assessed by physiotherapy on admission and discharge to inpatient rehabilitation including functional assessments of transfers and mobility, manual muscle testing, respiratory assessment (RPE and BORG scales, oxygen saturation), Timed up and Go, 10m walk, 6 minute walk test and Berg Balance Scale.

Results: Typically they have significant deconditioning related to often long standing illness and significant activity limitation prior to surgery, multiple and complex admissions and postoperative recovery and potential complications. On admission many patients are very debilitated and dependent requiring assistance to stand, transfer and mobilise, some requiring a hoist to transfer. Steroid induced and critical care myopathy are further complications Physiotherapy treatment focusses on increasing independence with functional tasks and mobility, improving muscle strength with graduated weight training, postural adaptations, altered patterns of breathing, improving static and dynamic balance and increasing cardiovascular fitness. This specialised patient population have extra problems to be considered including increased monitoring of vital signs during therapy, denervation of heart, immune-suppression and risk of organ rejection.

Conclusion: Patients responded well to physiotherapy intervention with improving independence, mobility, strength, balance and endurance. While the improvements are significant they are still below normal ranges.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>% of patients unable to do the test on initial assessment as too disabled</th>
</tr>
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<tbody>
<tr>
<td>Outcome</td>
<td>Average on admission to inpatient rehab</td>
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<tr>
<td>6 minute walk test</td>
<td>60.3m</td>
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<tr>
<td>10m walk test</td>
<td>29.9 secs (0.33m/sec)</td>
</tr>
<tr>
<td>Timed Up and Go</td>
<td>28.4 secs</td>
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<td>Berg Balance Scale</td>
<td>22.25/56</td>
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Immunosuppression and Trials & Surgical Techniques

ESTIMATION OF MYCOPHENOLIC ACID EXPOSURE POST RENAL TRANSPLANTATION: COMPARISON BETWEEN THE TRAPEZOIDAL METHOD AND MULTIPLE REGRESSION DERIVED LIMITED SAMPLING STRATEGIES.

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Background: The trapezoidal method is typically used in clinical practice for estimating mycophenolic acid (MPA) area under the concentration-time curve from 0-12 hours postdose (AUC0-12). However, this method can be inaccurate when the AUC0-4 profile is atypical. This study examined the performance of the trapezoidal method in estimating MPA AUC0-12. Concordance between trapezoidal and multiple regression derived limited sampling strategy (LSS) AUC estimations was assessed.

Methods: MPA samples were collected predose and at 1, 2 and 4 hours postdose in 157 kidney transplant recipients receiving tacrolimus and prednisolone co-therapy. MPA AUC0-12 was estimated using the linear trapezoidal rule and 7 previously published LSSs. AUC estimates were categorized into groups (<20, 20-40, 40-60, or >60 mg.h/L) and discordance in categorization between the 2 methods was assessed.

Results: The trapezoidal method was unable to estimate AUC0-12 in 26/157 (18%) due to a late or secondary Cmax (n=19) or high predose concentrations (n=7). Table 1 shows the absolute differences between trapezoidal and LSS estimates and the proportion of cases where the 2 methods resulted in different categorisation. AUC0-12 varied up to 4.8-fold depending on the LSS equation.

Conclusions: The trapezoidal method was unable to estimate AUC in a substantial number. Because wide differences exist between trapezoidal and LSS estimates in some patients, the 2 methods cannot be considered equivalent and shouldn’t be routinely substituted for each other in clinical practice. AUC estimates also vary widely depending on the LSS. To ensure accuracy, LSSs should be validated in the population of interest prior to use.
<table>
<thead>
<tr>
<th></th>
<th>LSS Equation 1</th>
<th>LSS Equation 2</th>
<th>LSS Equation 3</th>
<th>LSS Equation 4</th>
<th>LSS Equation 5</th>
<th>LSS Equation 6</th>
<th>LSS Equation 7</th>
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<tr>
<td>Minimum</td>
<td>0.10 mg.h/L</td>
<td>0.007 mg.h/L</td>
<td>0.02 mg.h/L</td>
<td>0.08 mg.h/L</td>
<td>0.05 mg.h/L</td>
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<td>2.6 mg.h/L</td>
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<td>Median</td>
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<td>5.9 mg.h/L</td>
<td>5.4 mg.h/L</td>
<td>6.5 mg.h/L</td>
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<td>11.3 mg.h/L</td>
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<tr>
<td>Maximum</td>
<td>40.2 mg.h/L</td>
<td>37.8 mg.h/L</td>
<td>20.3 mg.h/L</td>
<td>43.8 mg.h/L</td>
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<tr>
<td>Discrepant Categorisation</td>
<td>25%</td>
<td>37%</td>
<td>29%</td>
<td>37%</td>
<td>37%</td>
<td>37%</td>
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EVALUATION OF PREVIOUSLY PUBLISHED LIMITED SAMPLING STRATEGIES FOR ENTERIC-COATED MYCOPHENOLATE SODIUM IN ADULT KIDNEY TRANSPLANT RECIPIENTS

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Background: The aim was to evaluate the predictive performance of published limited sampling strategies (LSS) for estimation of mycophenolic acid (MPA) exposure (area under the concentration time curve, AUC) following enteric-coated mycophenolate sodium (EC-MS) in adult renal transplant recipients.

Methods: MPA concentrations were measured in 20 recipients (1 month posttransplant, receiving EC-MS twice daily). Samples were taken at 0, 0.33, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 8 hours and 0, 0.25, 0.5, 0.75, 1.0, 1.25, 1.5, 2.0, 3.0, 4.0, 6.0, 9.0 and 12.0 hours postdose on 2 sampling occasions a week apart. MPA plasma concentrations were determined using HPLC-MS-MS. Predicted MPA AUC were calculated using fourteen different LSS (5 reported studies) with data from the first sampling occasion for each patient, and compared to the second occasion full MPA AUC calculated from all measured concentration-time points using the linear trapezoidal rule. Bias (median prediction error [MPE]) and precision (root mean squared error [RMSE]) were calculated.

Results: Bias and precision (as % of median) for prediction of a future MPA AUC were <15% for 7 equations. Two equations using concentrations at 1, 3 and 9 hours and 1.5, 2.5, 3.5 and 6 hours post dose were superior to other models tested. Two equations using concentrations at 0.5, 1 and 3 hours and 1, 2, 2.5 and 4 hours post dose showed acceptable bias and precision.

Conclusions: Several LSS, including 2 used to develop equations with concentrations taken within 4 hours post-dose, predicted future MPA AUC after EC-MS with reasonable bias and precision.

RETROPERITONEOSCOPIC LIVE DONOR NEPHRECTOMY

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WA Liver & Kidney Transplant Service, Sir Charles Gairdner Hospital, Perth

Background: The aim of this study is to evaluate the outcomes of retroperitoneoscopic donor nephrectomy (RDN) in comparison with laparoscopic intraperitoneal approach (LIA).

Methods: From January 2010 to November 2015, 90 live donor nephrectomies were performed in our institute. Mean age was 50.98 years (26 – 75 years). Of 90, 34 were done by RDN whereas 56 were done by LIA. Operative time, graft warm ischaemic time, intraoperative and postoperative complications were recorded and analyzed. All forms of postoperative analgesia were converted to oral morphine equivalent for comparison. Kidney graft function was followed-up at 1 week, 3 months and 1 year post-surgery. Mean recipient age was 41.20 years.

Results: All donor nephrectomies were successfully performed with no conversions. There was no difference in operative time in both groups. No intraoperative complications were observed in both groups. No patients received blood transfusions. Mean graft warm ischaemic time was 4.34 minutes. There were 3 cases of chyle leak in RDN group and were managed conservatively. There was no significant difference in analgesia use in both groups. All kidneys were transplanted successfully and followed-up from 1 to 59 months. There was no delayed graft function and urological complications. Mean creatinine level at 3 months was 123.15.

Conclusion: RDN is an attractive alternative approach with comparable kidney graft function to LIA. This approach maintains the virgin abdomen for the donor and lowers the risk of intraperitoneal organ injury. The analgesic consumption in both groups was equivalent.
A QUALITATIVE REVIEW OF MEDICATION ERRORS MADE BY NEW KIDNEY TRANSPLANT RECIPIENTS

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Background: After kidney transplantation, patients are required to follow a complex and frequently changing medication regimen. Nonadherence to the prescribed schedule is associated with increased rates of rejection and graft loss, but detecting patients who make unintentional errors or who are intentionally nonadherent can be difficult. To assist with improving medication management in this group, the Renal Transplant Outpatient Pharmacist (RTOP) role was established.

To identify the rate and types of medication administration errors made by patients after renal transplantation; to explore reasons for these errors and to develop strategies to prevent further deviation from the prescribed regimen.

Methods: The RTOP reviews all new renal transplant patients in clinic after hospital discharge, providing medication education and early identification of medication errors. Medication administration errors were recorded in the nephrology patient database (Nephworks). Records were reviewed retrospectively for the first 50 transplant patients since the RTOP role was established to identify and characterise those errors.

Results: The RTOP identified numerous dangerous mistakes including: confusion over medication strengths leading to under and overdosing; tablets halved inappropriately; incorrectly packed dose administration aids; incorrect administration times and failure to make prescribed dosage changes.

Conclusions: Medication errors were common in the early post-transplant period. The majority of errors identified at this early stage were unintentional and related to poor medication knowledge, the complexity of the medication regimen and misunderstandings about changes.

SIROLIMUS PRECIPITATES INCISIONAL HERNIA IN TRANSPLANT PATIENTS

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Background: To examine the rate of hernia in abdominal transplant patients, and investigate immunosuppression effect.

Methods: Systematic review was utilized to investigate the rate of hernia in abdominal organ transplantation and compare rates between different organ transplants. We moderated by immunosuppression to investigate whether this played a role in moderating risk for hernia.

Results: 72 relevant articles were identified for systematic review and 51 individual studies contained statistics necessary for meta-analysis. This included 31,203 abdominal transplant recipients consisting of 18,686 kidney transplant recipients, 11,957 liver transplant recipients, 171 pancreas transplant recipients and 208 intestinal transplant recipients. In the remaining 181 patients, the organ transplanted was unclear or multi-organ transplantation occurred. Hernia in abdominal transplants occurred at an overall event rate of 0.06 (n=56, CI 95% 0.05-0.09, p<0.001). These effects were moderated by use of sirolimus with sirolimus associated with a 3 times higher rate of hernia (n=10, ER=0.18, CI 95% 0.10-0.29, p<0.001) compared with no sirolimus (n=24, ER=0.06, CI 95% 0.04-0.10, p<0.001). The rate of hernia was highest in liver transplants (n=29, ER=0.10, CI 95% 0.07-0.14, p<0.001) followed by intestinal transplant (n=3, ER=0.07, CI 95% 0.02-0.27, p=0.001), kidney transplants (n=22, ER=0.03, CI 95% 0.02-0.06, p<0.001) and pancreas transplants (n=3, ER=0.02, CI 95% 0.01-0.06, p<0.001).

Conclusions: The rate of hernia is low in transplant patients and varies by the type of organ transplanted, the rate being highest in liver recipients and lowest in pancreas transplants. Sirolimus greatly increases the rate of hernia formation.
RESTORED KIDNEY TRANSPLANTATION - EXTENDED CRITERIA DONORS
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Background: Many patients have a total nephrectomy to treat localised cancer, discarding a significant volume of normal kidney. Restored renal donation involves excising focal pathology after nephrectomy and transplanting the residual kidney. Existing reports describe excising small renal lesions, and the increasing popularity of partial nephrectomy has almost eliminated this donor source. We questioned the validity of only using kidneys with small cancers, and report our experience transplanting kidneys with larger renal cancers.

Methods: We used outcomes from partial nephrectomy to estimate cancer transplantation and complication rates for renal cancers of all sizes. We reviewed the cancers we were treating with total nephrectomy, and estimated the functional tissue in these kidneys. We used this information to obtain Clinical Governance and NSW State Transplant Advisory Committee approval to transplant restored kidneys after excising cancers up to 5 cm. Only older high risk recipients were eligible. All data and outcomes were recorded prospectively.

Results: 26 patients were referred for evaluation, and 20 proceeded to donation. Data is being collected continuously, including patient and graft survival, and operative complications. Urinary fistulae and urinary tract infection are the commonest complications. There is no 90 day mortality in recipients or donors. There has been 1 cancer recurrence attributable to transplantation with the kidney.

Conclusion: Renal cell carcinomas up to 5cm in size can be safely excised ex vivo, leaving adequate nephron mass to provide a viable transplant. Low complication rates and high graft function rates justify persisting with this technique.

COMBINATION OF LEFLUNOMIDE AND EVEROLIMUS FOR TREATMENT OF BK VIRUS NEPHROPATHY
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¹Nephrology and Renal Transplant, St Vincent's Hospital, Melbourne, ²Department of Anatomical Pathology, St Vincent's Hospital, Melbourne

Background: BK nephropathy (BKN) is 1 of leading causes of graft loss following renal transplantation, possibly due to newer immunosuppressive therapy. Currently minimization of immunosuppressive regimen is the first line of therapy but this needs to be balanced with the increased risk of rejection. In some cases, despite lowering immunosuppression, BK infection can persist and leads to graft loss. Recent in-vitro experiments demonstrate reduction in BK viral replication when infected cells are treated with the combination of Leflunomide and Everolimus.

This study aims to explore the effect of this drugs combination on viral clearance and graft function in patients with persistent disease despite reduction in immunosuppression.

Methods: We treated 3 patients with combination of Leflunomide and Everolimus. Data on medical history, biochemical parameters and viral loads were collected (Table 1).

Results: Significant improvement in viral loads was observed in 2 cases with resolution of viraemia in another (Table 1). Two recipients had preservation of allograft function. The remaining graft was lost due to combination of obstruction and BKN. No adverse reaction such as bone marrow toxicity was observed. One patient has elevated ALP level which correlates to moderate renal impairment.

Conclusion: Combination of Leflunomide and Everolimus is safe and should be considered as a rescue therapy in treatment of BKN, especially in those who fail to clear this infection despite reduction of immunosuppressive therapy.

| TABLE 1. Baseline characteristic and result of patients on combination of Leflunomide and Everolimus |
|-----------------|----------------|----------------|
| **Patient**     | **1**          | **2**          | **3**          |
| Gender          | F              | M              | M              |
| Age (years)     | 56             | 55             | 67             |
| Type of transplantation | Deceased donor | Kidney-Pancreas | Deceased donor |
| No of transplantation | 2nd graft      | 1st graft      | 1st graft      |
| Initial immunosuppression | Pred, MMF, Tac | Pred, MMF, Tac | Pred, MMF, Tac |
| Time to diagnosis (months post transplant) | 4              | 48             | 5              |
| Peak BK titre (copies/mL) | 40 million    | 6 million      | 9.3 million    |
| Histological classification on biopsy | Stage B3       | Stage B3       | Stage B3       |
| Baseline Creatinine (µmol/L) | 110 -120     | 80-100         | 170            |
| Peak Creatinine (µmol/L) | 300           | 150            | ESRF           |
| Current Creatinine (µmol/L) | 180           | 130-140        | ESRF on dialysis |
| Years since transplantation | 2             | 5              | 2              |
| Current BK titre (copies/mL) | undetectable  | 271,000        | <25,000         |

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COMBINED HEART AND LIVER RETRIEVAL AFTER CIRCULATORY DEATH WITH NORMOTHERMIC MACHINE REPERFUSION IN A PORCINE MODEL

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Transplantation Laboratory, Victor Chang Cardiac Research Institute, Sydney

Background: When donation after circulatory death (DCD) heart and liver retrieval are combined, there are concerns regarding delays to institution of liver cold preservation. We aim to develop a combined DCD heart and liver retrieval protocol in a pig model with subsequent normothermic machine perfusion (NMP).

Methods: Pigs (n=12; 60-70kg) were anesthetised. Baseline observations recorded. After sternotomy, and laparotomy, ventilatory support was withdrawn to mimic DCD conditions. Death was defined as equalisation of central venous and mean arterial pressures. After a 5-minute stand-off period, blood was collected from a right atrial cannula then cardiac preservation flush (4°C) commenced via the proximal ascending aorta. The inferior vena cava was vented. The thoracic cavity was kept cold with saline ice slush. The heart was explanted and prepared on back-table for NMP. Liver preservation begun immediately after blood collection by cold preservation solution flush via the infra-renal aorta. The hepatic artery, portal vein and common bile duct were transected, and the liver explanted for back-table NMP preparation.

Results: Warm ischaemic time (WIT) and back-table time (BTT) are presented in table below. The average blood volume collected was 1.6L; 1:1 dilution with Krebs resulted in significant hemodilution and hypocalcemia. This resulted in sub-optimal cardiac contractile recovery despite a favourable lactate profile. Liver enzyme release, bile production, and lactate and pH profiles were favourable during 4-6 hours of NMP.

Conclusions: Heart and liver retrieval under standard DCD protocol is possible without excessively extending the WIT for either organ. However, there is insufficient donor blood to support NMP of both organs.

<table>
<thead>
<tr>
<th>TABLE 1.</th>
<th>Heart</th>
<th>Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>WIT (Warm Ischaemic Time)</td>
<td>21 + 5min</td>
<td>20 + 6min (commencement of flush)</td>
</tr>
<tr>
<td>BTT (Back Table Time)</td>
<td>29 + 6min</td>
<td>33 + 19min</td>
</tr>
<tr>
<td>Blood Volume Collected</td>
<td>1621 + 279ml</td>
<td>33 + 19min</td>
</tr>
<tr>
<td>Hct</td>
<td>Baseline (Heart)</td>
<td>On Rig (Heart)</td>
</tr>
<tr>
<td>Hct</td>
<td>23 + 5%</td>
<td>15 + 6%</td>
</tr>
<tr>
<td>Ca²⁺</td>
<td>1.30 + 0.15mM</td>
<td>0.64 + 0.32mM</td>
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</tbody>
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