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NEW ASPECTS REGARDING NEOADJUVANT RADIOCHEMOTHERAPY IN LOCALLY ADVANCED NONINFLAMMATORY BREAST CANCER AND PREDICTIVE FACTORS FOR A PATHOLOGIC COMPLETE REMISSION

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Background:

Neoadjuvant radiochemotherapy (NRT-CHX) in locally advanced noninflammatory breast cancer (LABC) is still under debate. Long-term outcome data and predictive factors for pathologic complete response (pCR) were analyzed.

Patients and methods:

During 1991-1998, 315 LABC patients (cT1-cT4/cN0-N1) were treated with NRT-CHX. Chemotherapy was administered prior to RT in 192 patients, and concomitantly in 113; 10 patients received no chemotherapy. The update of all follow-up ended in November 2011. Age, tumor grade, nodal status, hormone receptor status, simultaneous vs. sequential CHX, and the time interval between end of RT and surgery were examined in multivariate terms with pCR and overall survival as end point.

Results:

The total pCR rate after neoadjuvant RT-CHX reached 29.2%, with LABC breast conservation becoming possible in 50.8% of cases. In initially node-positive cases (cN+), a complete nodal response (pN0) after NRT-CHX was observed in 56% (89/159). The multivariate analysis revealed that a longer time interval to surgery increased the probability for a pCR (HR 1.17 [95% CI 1.05-1.31], p < 0.01). However, in large tumors (T3-T4) a significantly reduced pCR rate (HR 0.89 [95% CI 0.80-0.99], p = 0.03) was obtained. Importantly, pCR was the strongest prognostic factor for long-term survival (HR 0.28 [95% CI 0.19-0.56], p < 0.001).

Conclusion:

pCR identifies patients with a significantly better prognosis for long-term survival. However, a long time interval to surgery (> 2 months) increases the probability of pCR after NRT-CHX.
MANAGEMENT OF MICROMETASTASIS FOUND ON SENTINEL LYMPH NODE BIOPSY USING OSNA IN PATIENTS DIAGNOSED WITH EARLY BREAST CANCER

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Background and aim:

This is a retrospective review of breast cancer patients diagnosed of axillary micrometastasis using One Step Nucleic Acid Amplification (OSNA) technique for Sentinel Lymph Node Biopsy (SLNB). Increased rate of detection of lymph node micrometastasis has been seen using OSNA. The clinical implications and prognostic significance of micrometastasis in the sentinel lymph nodes remain a controversial issue.

Method:

A retrospective review of breast cancer patients who had SLNB using OSNA at Royal Liverpool University Hospital (RLUH) and radiotherapy at Clatterbridge Cancer Centre (CCC) during the first year use of OSNA was conducted.

Results:

- 261 patients underwent SLNB using OSNA between 01/11/2012 and 31/10/2013. 80/261 (30.65%) patients were found to have micrometastasis.

- 31 of these 80 patients underwent ALND which revealed one micrometastasis in one further patient and no further macrometastasis.

- 47 of these patients had breast conserving surgery and were referred for radiotherapy (RT). 32 of these received axillary RT using extended tangential fields and 15 patients had RT to breast only.

Conclusion:

This study demonstrates that the incidence of axillary nodal involvement after the identification of micrometastasis alone on SLNB is very low suggesting that ALND or axillary radiotherapy may not be necessary in these patients.
This has the advantage of avoiding potential morbidity associated with axillary RT and also reducing the radiotherapy planning and treatment time for these patients. Based on the results of this study, breast RT protocol has been revised axillary radiotherapy for micrometastasis is not recommended at CCC.
SERIAL RESECTIONS IN METASTATIC BREAST CANCER

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Background and aims:
To demonstrate the benefits of serial resections for isolated metastases originating from breast cancer.

Methods:
A 55 year old patient was submitted to surgery 9 years ago for a ductal invasive breast carcinoma.

Results:
At that moment Madden mastectomy was performed followed by adjuvant chemotherapy. At a two year follow up she was diagnosed with a right upper lobe pulmonary metastasis. A right superior lobectomy was performed and the histopathological examination confirmed the presence of a breast cancer pulmonary metastasis; adjuvant chemotherapy was re-initiated followed by hormone therapy for the next 5 years. Six years after pulmonary resection an unique hepatic lesion involving the left lobe was diagnosed. A left sectorectomy was performed and the histopathological and immunohistochemical studies confirmed the same origin. At one year follow up after liver resection the patient reports no recurrent disease.

Conclusions:
Although metastatic breast cancer is usually associated with poor prognosis, cases presenting isolated recurrences seem to benefit most from surgical treatment even if serial lesions are diagnosed.
COSMETIC OUTCOME ASSESSMENT AFTER NEOADJUVANT RADIOCHEMOTHERAPY IN BREAST CANCER PATIENTS

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Background:

Neoadjuvant radiochemotherapy (NRT-CHX) is an innovative technique for the treatment of patients with locally advanced non inflammatory breast cancer (LABC). The aim of this study was to analyze the long term cosmetic outcome in breast conserving and mastectomy patients.

Patients and Methods:

From 1991 to 1998 a total of 315 LABC patients (cT1-cT4/cN0-N1) was treated with NRT-CHX. 160 patients received a breast conserving surgery (BCS) and 154 patients were treated with mastectomy (ME). One patient had no surgery. RT consisted of EBRT of 50 Gy to the breast and the supra-/infraclavicular lymph nodes (n=255) combined with an electron boost in 214 cases or a 10-Gy interstitial boost with (192)Ir afterloading before EBRT in n=101 cases. Chemotherapy with CMF and AC/EC was administered prior to RT (n=192), and Mitoxantrone (n=113); no chemotherapy (n=10). Cosmetic outcome was assessed by patient questionnaire, a panel evaluation of 5 independent investigators graduated in 4 grades + breast retraction assessment (BRA). Quality-of-life was assessed by EORTC QLQ-C30 and BR23 and late radiation side effects by LENT/SOMA scale.

Results:

In 64 BCS and 43 ME a long term follow up of the cosmetic outcome was possible. Most patients rated their overall cosmetics as 'excellent' or 'good' (94% BCS and 55.8% ME). ME in detail: excellent: 27.91%, good: 27.91%, moderate: 39.53% and bad 4.65%. No grade III or IV late side effects. Median BRA-score after BCS: 2.9. QLQ-C30 was rated 'excellent' or good in 82%.

Conclusion:

NRT-CHX is associated with good cosmetic outcome.
NEOADYUVANT HORMONOTHERAPY IN LOCALLY ADVANCED BREAST CANCER, POSMENOPAUSIC WOMEN WITH HORMONAL RECEPTORS POSITIVE

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Objective:
Present display the objective respond, frequency complete clinical response and pathological complete response with the use of induction hormone therapy in posmenopausal women with locally advanced breast cancer, (stages III).

Methods:
Hospital in Mexico; 80 patients with infiltrated breast cancer. Positive hormonal receptors, with Her2 and p53. Prospective study, randomized using: letrozol, exemestan, and anastrozol; tamoxifen. 36 months for objective responds. Patients, whom did not show response to neoadjuvant therapy, became treatment with radiotherapy. Patients, whom showed complete or partial clinical respond, went candidates tomastectomy. Chi-2, with $p$ of Mantel-Haenzel table used to evaluate differences.

Results:
5 years, January of the 2009 to January of the 2013, the age average was 66.5 years old, with a rank of 45 to 75 years with breast cancer, FIGO stages III. Objective respond, OR=55%, 44 patients; Clinical respond, 32 patients (40%); CIR plus CPR, complete pathological respond, 12 patients (15%), $p=0.05$; Complete pathological respond was founded in 12 patients (15%); 40% with aromatase inhibitors and with tamoxifén TMX, 15%, $p=0.05$. Without Clinical respond (<50% tumoral volume) in eleven patients: 5 patients; 25% in tamoxifen group and 19% in patients with aromase inhibitors group, $p=0.05$.

Conclusions:
- HTNA is a good therapeutic alternative in posmenopausal women with locally advanced breast cancer, whom didn’t accept chemotherapy.
- Work shows efficacy of the HTNA for identify patients with breast cancer and hormonal receptors positives, without over express the protein HER2 and p53, they have better survive prognosis and could be rescue with mastectomy.
TREATMENT AND OUTCOME OF STAGE I A1 SQUAMOUS CARCINOMA OF THE CERVIX: A CLINICOPATHOLOGIC STUDY OF 346 CASES

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Background and aims:
To analyze the clinicopathologic feature of stage I A1 squamous carcinoma of the cervix (SCC) and explore the outcome of different surgical methods.

Methods:
Clinicopathological data of 346 cases with stage I A1 SCC diagnosed between November 2nd 1995 and December 31st 2011 were reviewed and analyzed. To figure out the change of its treatment, analyze the prognosis of various treatments and cases with lymphovascular space invasion (LVSI).

Results:
(1) The trend in treatment methods from 1995 to 2011 reveal that more and more cases were treated with CKC, MRH reduced obviously, while the proportion treated by TH remained unchanged. Due to a small number of cases received VT and RT, we did not detect any obvious changes. (3) Prognosis: The overall survival rate was 99.0%, and the overall recurrence rate was 1.2% (4/346). Both patients with distant metastasis died, resulting in case fatality rate at 0.6% (2/346). The overall survival rates for CKC, VT, TH, MRH, and RT were 100%, 100%, 98.2%, 100%, and 100%, the difference was not statistically significant (P=0.819). The overall survival rates for patients with LVSI and without LVSI were 99.3% and 93.3% respectively, and there was statistical difference between them (P=0.003). Univariate analysis showed that only LVSI was an important predictor for survival (P=0.030).

Conclusions:
The treatments for stage I A1 SCC are becoming more conservative, and individualized therapy and more frequent surveillance should be administrated to those patients with LVSI, since LVSI is an important predictor for prognosis.
Aim:
There is evidence that the mineral zinc is involved in apoptotic cell death of the various carcinoma cells. In this study, we aim to see whether zinc in the form of CIZAR induce apoptosis on cervical carcinoma cells by increasing intracellular zinc concentration.

Methods:
CaSki, HeLa cervical carcinoma cells and HPV-16 DNA transformed keratinocyte (CRL2404) were treated with different concentrations of CIZAR. Cell viability test and intracellular level of zinc were determined and apoptosis was confirmed by flowcytometry after propidium iodide (PI) staining and fluorescence microscopy under DAPI staining. Expression of cell cycle regulators were analyzed by Western blot including knock down of p53 and expression of HPV E6 and E7 genes by RT-PCR.

Results:
Intracellular zinc accumulation induced the down-regulation of E6/E7 proteins through targeting for the specific transcriptional factors in the upstream regulatory region. p53 were induced after treatment of CIZAR and p53-dependent apoptosis was not occurred after knock down by p53 siRNA. In cervical carcinoma cells regardless of HPV-infection, CIZAR induces apoptosis by activation of the p53-independent pathways through the up-regulation of p21Waf1, the down-regulation of c-Myc, and also decreasing the Bcl-2/ Bax ratio.

Conclusion:
In conclusion, CIZAR induces apoptosis not only through the restoration of p53/Rb-dependent pathways on HPV-positive cells but also through the activation of p53/Rb-independent pathways and the mitochondrial death-signal pathway on cervical carcinoma cells regardless of HPV-infection.
THE VALUE OF CYTOKERATIN 19 AND HUMAN PAPILLOMA VIRUS DNA AS MICROMETASTASIS MARKERS IN CERVICAL CANCER PATIENTS WITH INTERMEDIATE RISK FACTORS


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Background and aims:
This study aimed to evaluate the value of cytokeratin 19 (CK19) and human papilloma virus (HPV) DNA as micrometastasis markers in cervical cancer patients with intermediate risk factors.

Methods:
Polymerase chain reaction for HPV DNA and immunohistochemistry for CK19 were performed on 318 lymph node samples from 67 cervical cancer patients with intermediate risk factors.

Results:
HPV DNA and CK19 were detected in 23.5% (75/318) and 2.8% (9/318) of lymph nodes, respectively. Among the 67 patients, HPV DNA was detected in at least one lymph node from 31 patients (46.3%), while CK19 was expressed in 5 patients (7.4%). The five-year disease-free and overall survival rates were 90.5% in the CK19- or HPV DNA-positive group and 76.8% in the negative group (P = .47 and P = .59, respectively). There was no correlation between disease-free survival and CK19 or HPV DNA positivity (P = .92 and P = .83, respectively).

Conclusions:
The presence of HPV DNA in lymph nodes is not useful as a micrometastatic marker in cervical cancer patients with intermediate risk factors, while the value of CK19 expression requires further study in a larger sample population.
Background and aims:
This study aimed to compare surgical outcomes and effects on health-related quality of life (HRQOL) of patients who had undergone total laparoscopic (TLRH) versus total robotic radical hysterectomy (TRRH) for cervical cancer.

Methods:
This study included 73 patients who had undergone TLRH (n = 34) or TRRH (n = 29) between January 2010 and June 2014. Surgical outcomes and HRQOL were compared between the two groups. Pre- and postoperative HRQOL data from Short Form (SF-36) and European Organization Research and Treatment of Cancer Quality of Life-C30 (EORTC QOL-C30) questionnaires were recorded for all of the patients.

Results:
In the TRRH group, there were more cases of para-aortic lymphadenectomy (p < 0.01), longer operation time (p < 0.01), less estimated blood loss (p < 0.01), and more harvested pelvic lymph nodes (p = 0.04). Overall, all of the SF-36 scale scores except Physical Functioning improved after surgery, while all of the EORTC QOL-C30 functional and symptom scale scores but Global QOL status and Nausea/Vomiting and Pain improved after surgery. There were no significant differences in any of the changes in functional and symptom scales or items of the SF-36 and the EORTC QOL-C30 between the two groups. However, there were strong correlations and statistical significance seen between SF-36 and EORTC QOL-C30 score pairs.

Conclusions:
TRRH surgical outcomes showed less blood loss and more harvested pelvic lymph nodes but longer operation times with statistically significant differences. The short-term postoperative HRQOL outcomes did not show significant intergroup differences.
ATYPICAL HEPATECTOMY FOR LIVER METASTASES FROM CERVICAL CANCER

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Background and aims:
Cervical cancer is still an important health problem affecting many women worldwide. Although liver metastases are not frequently seen, their presence is usually associated with poor survival.

Methods:
We present the case of a 62 year old patient diagnosed with cervical squamous cell carcinoma with pelvic and para-aortic adenopathies and a solitary liver metastasis.

Results:
A total radical hysterectomy with bilateral adnexectomy, pelvic and para-aortic lymph node dissection (picture 1) and atypical hepatectomy (picture 2) were performed. The histopathological examination confirmed the presence of a well differentiated squamous cell carcinoma and demonstrated the same origin for the liver lesion. At a two year follow-up the patient is free of any recurrent disease.

Conclusions:
Although the presence of liver metastases classified the case as a IVB cervical cancer, a radical surgical approach seemed to be perfectly justified and an important survival benefit was obtained.

Picture 1: the final aspect after pelvic resection
Picture 2: atypical hepatectomy for cervical cancer liver metastasis
HYPOXIA AND BIOMARKERS EXPRESSION IN CERVICAL CANCER (CC) AND HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESIONS (HSIL)

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Background:
Tumor Hypoxia is a critical factor in cancer progression and therapy response. It induces Hypoxia Inducible factor (HIF1α), Vascular Endothelial Growth Factor (VEGF), Carbonic Anhydrase IX (CAIX) and Glucose Transporter 1 (GLUT1). New biomarkers are necessary to improve conventional treatments.

Objectives:
To determine the expression and prognostic value of HIF-1α, VEGF, CAIX and GLUT-1 in CC FIGO stages Ib2-Ilb and in HSIL.

Methods:
A retrospective study was performed in 100 patients with CC, 40 HSIL and 40 normal tissues (Database 1987-2005). Expression was examined by immunohistochemistry and analyzed according Immunoscore.

Results:
HIF-1α was expressed in 64% CC while only weakly in 10% HSIL (p<0.05). No normal samples express HIF-1α. Higher number of CC expressed VEGF compared to HSIL (75% vs 50% p<0.05); HSIL was also higher vs normal samples (20/40 and 10/40 p<0.001). CAIX was detected in 70% CC, In HSIL, positive expression was detected in half of the samples, being lower than in CC (50% vs 70%). CAIX was never detected in normal cervix. GLUT1 was highly expressed in CC vs HSIL (90% vs 45%, p<0.05). GLUT1 was absent expressed in normal tissues. No correlation was found between CAIX, VEGF and GLUT1 expression with overall survival. HIF1α correlated with lower survival measured at 24 months evolution.

Conclusion:
Our data showed a significant increase in the expression of biomarkers from the premalignant lesion up to the invasive stages. No marker could be considered as independent prognostic factor for CC.
Introduction:
Para-aortic nodal status in uterine cervical cancer (UCC) has both prognosis and treatment implications. These patients have been traditionally managed with extended field radiotherapy with or without concomitant chemotherapy, a treatment modality associated with significant morbidity. Recently 18-fluoro-2-deoxy-D-glucose positron emission tomography (FDG PET) has emerged as a highly accurate tool to identify extrapelvic disease; however, it has been reported a false-negative rate up to 20% within the retroperitoneal nodal basin. The goal of this study was to assess FDG-PET performance for the detection of para-aortic lymph node (PALN) metastasis in women with early bulky as well as locally advanced uterine cervical cancer (LAUCC).

Method:
Women with FIGO stages IB2 to IIIB (UCC) managed in our institution between 2012 and 2015 were prospectively recorded. All of them underwent both pretreatment FDG-PET and subsequent laparoscopic PALN sampling. Sensitivity, specificity, positive and negative predictive values and likelihood ratios were estimated on the basis of imaging and pathological findings.

Results:
A total of 23 patients were identified. All of them underwent laparoscopic lymphadenectomy up to the inferior mesenteric artery. Sensitivity, specificity, positive and negative predictive values and positive and negative likelihood ratios of the FDG-PET were 66.67, 95, 66.67, 95 , 13.33 and 0.35, respectively, for the detection of PALN involvement.

Conclusions:
Conversely to was previously published, our study suggested that staging FDG-PET exhibits high diagnostic accuracy in detecting PALN involvement among patients with early bulky/LAUCC. Further studies are needed to identify risk factors associated with false-negative results.
Background:
In Chile, incidence of cervical cancer (CC) estimated in 2008 was 1,000 new cases. The mortality rate was 7.5 per 100,000 women and the adjusted rate was 5.9 per 100,000 women. An estimated 48.4% of deaths occur between 35 and 64 years.

Aim:
To describe the overall survival in patients diagnosed with CC between 2009 and 2013 and secondarily overall survival according to stage and histology.

Material and Methods:
Case series. Inclusion criteria were patients admitted to National Cancer Institute diagnosed with CC by histological type squamous cell carcinoma and adenocarcinoma, from 2009 to 2013, belonging to the macro public service network. We excluded women with second primary cancer recurrence since 2009. Survival analysis was expressed by Kaplan Meier method and survival curves were compared using the log-rank test. Statistical software used was Stata 12 ®. A confidence level of 95% was considered.

Results:
453 patients were analyzed. 83.22% (377) had squamous histology, 67.13% (57) adenocarcinoma and 64.29% (14) other histology. 35.76% (162) were stage II and 38.19% (173) had stage III, constituting both the 73.95% of cases. Overall survival was 67.05% at 5 years. Median follow-up was 2.57 years (1386-3882). According histology, overall survival was 67.33% for squamous, 67.13% adenocarcinoma and 64.29% for others. Overall survival for the different stages was: 90.40% (93) for I, 77.80% (162) for II, 47.42% (173) for III and 26.45% (19) for IV. Statistically significant differences were presented as stage of disease.

Conclusion:
Overall survival CC was 67.05% at 5 years, with statistically significant differences by stage.
Uterine cervical cancer is a prevalent neoplasia. 30% of patients will have recurrence during the following, presenting bad prognosis with survival rates lower than 15-20% on the first year. To date there’s no evidence of good quality following. The main objective was to know this cancer’s pattern of recurrence.

Materials and methods:
Retrospective study including all patients treated and followed at Higuera Hospital from 2003 to 2014. Patients included, were those having first treatment with curative intentions indicated by a committee and with evidence of complete response to it, and histology diagnosis, not depending on histology type and FIGO stage.

Results:
292 patients signed in, 78 were excluded by protocol, and 214 analyzed. 31 recurrences where found (14.4%). Medium age of diagnoses was 50.7 years. Of these patients, 27 received radiation and 4 surgery as primary treatment. IIB was the main staging with 11 cases. Average disease-free interval was 12.3 months. 41.9% had LVI (+), of which 90.3% were squamous cell carcinoma. The dominant histological grade was II with 15 cases (48.3%). Tumor size was informed in 30 patients, the average size being 5.4 cm. There were no cytologic diagnoses. 68% were symptomatic. Diagnosis was clinical in 28 cases (90.3%), with Vaginal discharge or bleeding being the most frequent signs with 8 cases (38%). 19 were locoregional, 7 systemic and 4 combined. As of localization, 20 were pelvic, 4 on lymph nodes, and 2 in the cupula, with pulmonary and bone lesions being less frequent.

Conclusion:
Recurrences in cervical cancer are mainly early, symptomatic and pelvic. Clinical exam is Key to diagnoses.
Inquest and handling of preinvasive cervical lesions are key in cancer mortality decrease in general population. Adequate cyto-colposcopy-histology allows optimum pathology management. The main Objective was to determine cytological and clinical correlation with final histological HSIL.

Materials and methods: retrospective study including all patients referred to CPU in Higueras Hospital because of altered cytology or suspicious cervix between 2003 - 2014. All patients referred and evaluated by a specialist were included. Patients without biopsy were included for statistic calculus purposes. Results: 3928 patients were signed in and analyzed, of which 3117 were analyzed for cytology and 811 for suspicious cervix. 521 didn’t have biopsy. 1033 referrals were because of LSIL (26.2%) and 849 because of HSIL (21.6%). 21.8% of CIN I, 55% of CIN II and 68.2% of CIN III cytologies had final HSIL histology. Invasive cancer rates in these histologies were 1%, 2.3% and 8.8%, respectively. According to atypical cytology, 13.9%, 32.7%, 7% and 41.1% of respective correlation with PAP smear ASCUS, ASC-H, AGC - suggestive of reactive endometrial origin and AGC – suggestive of malignant neoplasia were found. Suspicious cervixes presents a 21.7% of high grade lesions and 15.2% of invasive lesions in the final biopsy. Conclusion: HSIL cytology present high histological correlation. ASC - H and AGC atypical PAP are more frequently associated with high grade lesions and require thorough colposcopic and histologic evaluation.
Background and aims:
Cervical uterine cancer (CC) is the third cause of death from cancer in women. CC requires persistent infection with human papillomavirus. The primary screening of CC is the Pap test, but its sensitivity and specificity is variable. The use of specific biomarkers has been a challenge to increase the sensitivity of the diagnosis. In this sense, we built tissue microarrays (TMAs) and assessed the protein expression level of 20 molecules from the Notch signaling pathway and tumorigenesis for the evaluation of early biomarkers.

Methods:
TMAs contained cores of 18 cervical normal tissue, 83 cervical intraepithelial neoplastic lesion (CIN)1, 53 CIN2, 28 CIN3 and 23 malignant tumors. Immunohistochemistry was performed with monoclonal/polyclonal antibodies and the SuperPicture 3rd Gen IHC kits from Invitrogen. Cores were examined and photographed with a Leica-DM750 microscope. Images were processed with the free ImageJ software and data analyzed by using the R software.

Results:
Statistical analysis showed SEL1 and Notch3 proteins to have a key sustained expression pattern (HSD groups, Table 1) against normal tissues (Figure 1).

Conclusions:
The Notch-3 receptor is a key component in the control of cell fate during development while SEL1 is a negative regulator of these receptor family, hence alterations in this pathway can contribute to tumorigenesis. We suggest SEL1 and Notch-3 proteins are potential biomarkers in CC.
Table 1. Summary of statistical data

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Figure 1. Protein expression data of SEL1 and Notch-3 in normal tissue (N), CIN 3-3 (II, II, III) and malignant tumor (T).
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Cervical Cancer

EVALUATION OF RESIDUAL DISEASE IN HYSTERECTOMY SPECIMENS AFTER CONIZATION IN WOMEN TREATED FOR SQUAMOUS MICROINVASIVE CARCINOMA OF THE UTERINE CERVIX
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Objective:
To assess the prevalence of residual disease in hysterectomy specimens after conization in women treated for squamous microinvasive carcinoma of the uterine cervix (MIC).

Methods:
A cohort of 299 patients with MIC diagnosed and treated at Campinas State University, Brazil was analyzed. All patients underwent cervical conization and of these, 158 followed by hysterectomy. Endocervical margin status of the cervical conization and the presence of residual disease in the hysterectomy specimens were analyzed.

Results:
103 of 158 conization specimens had positive endocervical margins (CIS=96/MIC=7), 51 were negative and 4 had non evaluable margins. In hysterectomy specimens 92 cases had residual disease (CIS or MIC) and 66 were free. In 96 conization specimens with endocervical margins positive for CIS, 44 (45.8%) had CIS, 27 MIC (28.2%) and 25 (26%) no residual disease in hysterectomy specimen. In the 7 conization margin positive for MIC: 2 had CIS (28.5%), 3 had MIC (43%) and 2 no residual disease (28.5%). Residual carcinoma/CIS in the hysterectomy is highly associated with positive endocervical conization margins (p<0.0001). On the other hand, in 51 cases of free conization endocervical margins, 14/51 (27.4%) had residual disease: 11 CIS (21.6%), and 3 MIC (5.8%).

Conclusions:
Positive endocervical margins are highly associated with residual disease in hysterectomy specimen (73.8%) so further treatment is mandatory. Conservative treatment should be carefully evaluated, and close follow up should be done even in patients with free conization margins because almost one third of the patients had residual disease in hysterectomy specimen.
SURVIVAL IN CERVICAL CANCER PATIENTS TREATED BY MINIMALLY INVASIVE SURGERY

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Background and Aims:
Laparoscopic-vaginal radical hysterectomy (LVRH) is accepted for the treatment of cervical cancer, with a smaller incision, reduced blood loss, quicker recovery, and same survival compared with laparotomy. The aims were to determine 2 and 5-year survival in cervical cancer patients treated by LVRH and to compare with series by radical abdominal hysterectomy by laparotomy (RAH) and to determine the average of lymph nodes in both series.

Methods:
Concurrent cohort study (group 1) and retrospective case control study (group 2). Patients with cervical cancer FIGO stage Ia2, Ib1 and IIa (≤ 2cm) submitted a LVRH, from 2001 to 2007 (group 1, n=64), and submitted a RAH from 1995 to 2007 (group 2, n=108). The laparoscopic time consisted of pelvic lymphadenectomy, cauterization and section of uterine vessels, preparation of vesical and pararectal spaces, parametrectomy and salpingectomy. The lymph nodes were sent separated, left and right sides, to the pathologist. Age, tumor size, histologic type, number of lymph nodes, metastasis and complications were registered.

Results:
The 2 and 5 years-survival in group 1 patients were 98 and 96.2%, and, in group 2, were 89.8 and 84.3% (p=0.09 and 0.2). General 2 and 5 years-survival were 92.8 and 88.3%. The average of lymph nodes by laparoscopy was 23.1 and, by laparotomy, was 21.7.

Conclusions:
The 2 and 5-year survival of cervical cancer patients treated by LVRH were similar to patients treated by RAH. The average of lymph nodes by laparoscopy was greater than laparotomy, without significant difference.
DISEASE RECURRENT AFTER LOOP TREATMENT FOR HIGH GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA

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Backgrounds and Aims:
Purpose of cervical cancer screening is to detect cervical intraepithelial neoplasia (CIN) and to treat it before cancer. Treatment involves surgical excision, to exclude unsuspected invasive cancer. Besides that, positive margins can determine adequacy of treatment. The aim of this study was to evaluate association of margin status and other clinical and pathologic factors with disease recurrence in patients treated with electrosurgical treatment.

Methods:
A cohort of 380 patients who underwent cervical conization due to CIN 2/3 diagnosed and treated at Campinas State University, Brazil was analyzed. Patients were followed for 24 months after procedure and excluded if didn’t attend at least one follow up visit. Recurrence was defined as any evidence of CIN 2/3, microinvasive or invasive cancer at follow-up. Univariate and Multivariate analysis were used to define predictive factors of recurrence.

Results:
380 cases were analyzed. Median age was 33.7 years. Histology revealed 50% CIN3, 25% CIN2, 13% CIN1, 3% microinvasion and 2% of invasive carcinoma. Endocervical margins were positive in 18%, ectocervical in 29% and both margins in 6%. Recurrence rate was 13%, with median interval of 15.5 months. Recurrence was related to history of 2 or more sexual partners (p=0.014) and positive endocervical margins in conization specimens (p=0.0099).

Conclusions:
Incomplete excision of CIN exposes women to major risk of recurrent disease. When margins are compromised a second procedure is recommended. Close follow up for the initial 24 months is required since the risk of recurrence is higher in this period.
Background:
Pregnancy complicated by cancer is relatively rare, however its incidence has increased. This is attributed not only to higher rates of cancer in general, but also to a delay in childbearing to the third and fourth decades of life. Cervical cancer (CC) is one of the most common gynecologic malignancy associated with pregnancy with an incidence ranging from 1-10 per 10,000 pregnancies. In Chile there is no data about incidence of CC in pregnant patients, but it is estimated that an oncology referral center should treat at least one case per year.

Aim:
The objective of the study was to analyze the clinical features of cervical cancer in pregnant patients treated in a regional Chilean center.

Methods:
Retrospective case series of patients with cervical cancer diagnosis during pregnancy, treated in Carlos Van Buren Hospital (Valparaiso - Chile), during 2014.

Results:
Of 2800 deliveries, three patients were identified with CC, all were multiparous, with mean age of 36 years. All deliveries were at term and by cesarean section. One patient had pre-pregnancy diagnosis of cervical cancer stage IB1 and was treated with vaginal radical trachelectomy with laparoscopic lymphadenectomy. Two patients had persistent vaginal bleeding during pregnancy, and were diagnosed during third trimester, (stage IIA and IIB), and were treated post-partum with radio and chemotherapy. All women are in follow-up with no visible tumor.

Conclusions:
Pregnancy represents an exceptional opportunity for the early diagnosis of cervical cancer, however, in our center it is still a late diagnosis.
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POSITIVE MARGINS IN COLD KNIFE CONE: PREVALENCE AND RESIDUAL LESIONS
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Objectives:
To identify the frequency of positive margins in surgical specimen of cold knife cone (CKC) for cervical intraepithelial neoplasia (CIN) and to analyze the edges and the residual tumor in the surgical specimen of second procedure.

Methods:
Retrospective cohort study in the Gynecology Department of Hospital Santa Casa Porto Alegre. Patients who had a diagnosis of cervical intraepithelial neoplasia (CIN) II/III and underwent CKC between April 2004 and December 2013.

Results:
484 patients underwent CKC during this period. Twenty one patients with invasive disease were excluded, resulting in 463 patients. Positive surgical margins were found in 100/463 patients (21.5%), 11% of them with positive ectocervical margins, 71% with positive endocervical margins and 18% with both. The pathology results were CIN II/III in 89%, CIN I 7%, and adenocarcinoma in situ 4%. In the 100 patients with positive margins, 58 underwent a new procedure. In the second procedure, pathology results were: invasive disease 1,7%, adenocarcinoma in situ 1,7%, CIN II/III 51.7%, CIN I 15,5%, and with no lesions, 29.3%.

Conclusions:
The frequency of positive margins, in our study, was an accordance to the literature, but we have observed a greater involvement of the endocervical margins and a higher prevalence of CIN II/III. Among the patients who underwent a second procedure we found a prevalence of 70,7% residual lesions.
LAPAROSCOPIC RADICAL TRACHELECTOMY: TECHNIQUE, FEASIBILITY AND OUTCOMES. EXPERIENCE HOSPITAL ITALIANO BUENOS AIRES, ARGENTINA

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Objectives:
To describe our surgical technique for laparoscopic radical trachelectomy, to evaluate its feasibility and show the perioperative results at Hospital Italiano de Buenos Aires, Argentina.

Material and Methods:
We analyzed 10 patients who underwent laparoscopic radical trachelectomy for early-stage cervical cancer between December 2011 and Nov 2014.

Results:
10 patients were included. Total laparoscopic radical trachelectomy was performed in all cases. The mean age was 29 years old (range, 19-39), the mean BMI was 24 (range, 18-48) and the mean length of hospital stay was 40 hours (range, 24-72). The mean of operative time was 232 minutes (range, 180-300) and no intraoperative complications were reported. During the postoperative period two patient presented vulvar edema (which resolved spontaneously), two patient presented bladder dysfunction, one patient an acute retention of urine, one an urinary infection y one general fever. Pelvic and parametrial lymph nodes, vaginal cuff and cervical resection margins were negative for malignancy in all cases. 16 pelvic lymph nodes were removed in average (range, 10-25). Tumor stage was IB in 8 patients, was IA2 in one patient and was IIA1 in one patient. The mean tumor size was 15 mm (range, 7-30 mm). No patient required conversion to laparotomy.

Conclusions:
We consider that laparoscopic radical trachelectomy, performed by trained surgeons, is a feasible and safe therapeutic option, as a fertility-sparing surgical technique, with good perioperative outcomes for women with early-stage cervical cancer with fertility desire. Minimally invasive surgery provides the widely known benefits of this type of approach.
VAGINAL RADICAL TRACHELECTOMY. A 10 YEARS EXPERIENCE OF 3 CENTERS IN CHILE

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Introduction:
Cervical cancer is the second most common cancer in women worldwide, being responsible of 275,008 deaths per year. In Chile, 1000 new cases are expected per year, of which 68.3% will be diagnosed in stage FIGO I-II. 37% of the cases present in women under 45 years old. Fertility-sparing surgery, such as radical trachelectomy can be safely performed, in terms of oncologic outcomes. We report the experience of 3 national institutions. A description of patients and oncologic outcomes is made on women treated with vaginal radical trachelectomy

Methods:
A retrospective review of oncologic outcomes was performed in patients who underwent vaginal radical trachelectomy, between April 2004 and September 2014.

Results:
A total of 28 radical trachelectomies were performed. 25 of them were classified stage FIGO IB₁, 1 was IA₁ and 2 others IA₂. In terms of histology 16 had squamous and 12 had adenocarcinoma. Average age was 30 years. The median follow-up was 54 months. No parametrial or vaginal involvement was detected in final pathology. One patient had lymph node involvement, and received adjuvant chemoradiation. Lymphovascular space invasion was present in 4 patients. One postoperative complication was reported (Vesicovaginal fistula). 3 patients had a recurrence, at 12, 24 and 30 months of follow-up. 9 women conceived a total of 11 live births.

Conclusion:
Radical trachelectomy appears to produce similar oncologic outcomes to those after radical hysterectomy, and has the benefit of preserving fertility.
EVALUATION OF CONE DEPTH TO ACHIEVE NEGATIVE MARGINS AFTER ELECTROSURGICAL TREATMENT FOR HIGH GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA
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Backgrounds and Aims:
Loop electrosurgical excision procedure (LEEP) is widely accepted for diagnosis and treatment of high grade cervical intraepithelial neoplasia (HGCIN). Positive margins of conization specimen have been reported to be the most important predictor of residual disease and disease recurrence in these patients. The aim of this study was to evaluate appropriate cone depth for predicting margin status and risk of recurrent disease after LEEP treatment.

Methods:
Analysis of medical records of 380 patients who underwent LEEP due to CIN 2 or CIN3 from January 2009 to December 2010 at CAISM-Unicamp.

Results:
380 cases were analyzed. Endocervical margins were positive in 18 %, ectocervical in 29 % and both margins in 6%. Recurrence rate was 13% (48/380), with median interval of 15,5 months. Positive endocervical margins were related to recurrence (p=0,0099). Positive ectocervical margins were not statistically related to recurrence (p= 0,3445). Depth analysis revealed that specimen with depth > 17 mm were related to lower risk of positive margins. The relation between depth of cone and recurrence risk was not clear.

Conclusions:
These findings suggest that disease at endocervical margins are related to higher risk of recurrence so it is mandatory to consider depth of specimen when planning a LEEP procedure. When performing a LEEP, colposcopists should aim for > 17 mm of depth, as to achieve oncologically safe limits and outcomes.
LAPAROSCOPIC POSTERIOR EXENTERATION IN CERVICAL CANCER: INITIAL EXPERIENCE AT HOSPITAL ITALIANO DE BUENOS AIRES

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Objective:
To describe the technique, feasibility, and morbidity of laparoscopic posterior exenteration in one patient with advanced cervical cancer.

Introduction:
Pelvic exenteration has both a palliative and curative role in the management of cervical cancer. It is important to identify which patients could benefit from this radical procedure and be relieved of severe and limiting symptoms.

Patients:
We describe a 38 year-old woman diagnosed with neuroendocrine cervical carcinoma, FIGO stage IIB. She received concurrent chemoradiation to the pelvis with cisplatin and etoposide, followed by high-dose-rate intracavitary brachytherapy, achieving complete clinical response. After ten months of follow up, magnetic resonance imaging revealed a rectal mass of approximately 2 cm. The lesion was hypermetabolic and suggestive of metastatic disease by PET-CT (SUV 9). Since there was no other evidence of disease, laparoscopic posterior exenteration involving selective resection of the uterus, adnexae, vagina, and rectum was performed. A five port approach which included use of harmonic shears, LigaSure device, and a circular endostapling instrument was used. There were no intraoperative complications. The time of surgery was seven hours and three units of blood were required. The hospital stay was 13 days. The patient developed a wound infection, and antibiotics and evacuation under CT was required. The pathology specimen had satisfactory margins. Six months into follow up, the patients remains without evidence of disease.

Discussion:
Laparoscopic aproach for posterior exenteration seems feasible in selected advanced gynecologic cancer. Larger studies with follow up are still needed to confirm the benefits, but recent data is promising.
TREATMENT OUTCOMES OF PATIENTS WITH EARLY STAGE CERVICAL CANCER TREATED WITH LAPAROTOMY COMPARED TO ROBOTICALLY ASSISTED LAPAROSCOPIC APPROACH

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Objective:
We evaluated the treatment outcomes of patients with early stage cervical cancer treated by laparotomy compared to robotically assisted laparoscopic approach

Method:
Retrospective analysis of patients’ charts of early cervical cancer treated surgically from January 2003 to December 2014, were reviewed. Age, body mass index, FIGO staging, final pathology, blood loss, intra and post operative complications, mean hospital stay, lymph node yield, surgical margin, duration of follow up, reoccurrence, need for adjuvant radiation/chemotherapy were documented and compared. In total 34 cases were reviewed, 17 cases of robotic assisted radical hysterectomy compared to 17 cases of abdominal radical prior to the implementation of the robot for the treatment of early cervical cancer.

Results:
There was no statistical significance found in the demographics of age, BMI, past medical history or past surgical history when comparing the laparoscopic and laparotomy groups. When the histology was analyzed, 12 of the laparotomy and 11 of the robotic group had moderately differentiated squamous cell carcinoma. 1 of the robotic group had papillary serous carcinoma. 1 of the robotic had poorly differentiated squamous cell carcinoma. 5 of the laparotomy group and 4 of the laparoscopic group had adenocarcinoma.

Staging showed 5 in the robotic group and 5 in the laparotomy group with stage 1 A1 and 1A2. 11 in the laparoscopic group and 11 in laparotomy group with 1B1. 1 in the laparoscopic group and 1 in the laparotomy group with stage 2A.

Those treated with robotic laparoscopic surgery had an average hospital length of stay of 2 days in comparison to 10 days in the laparotomy group, with a p value of 0.0001. The blood loss for the laparoscopic group was 130cc when compared to 612cc in the laparotomy group, with a p value of 0.001. The blood transfusion rate intraoperatively in the robotic group was 0 when compared to 3 in the laparotomy group, with a p value of 0.07.
Post-operative complications include: ileus (0 in robotic, 1 in laparotomy), pulmonary embolus (0 in robotic, 1 in laparotomy), pulmonary edema (0 in robotic, 1 in laparotomy), PVC (1 in robotic, 0 in laparotomy), febrile morbidity (0 in robotic, 4 in laparotomy), fistula (0 in robotic, 1 in laparotomy) and incisional hernia (1 in robotic, 2 in laparotomy). The postoperative complications yielded a p-value of 0.03.

The nodal yield (11 robotic, 14 laparotomy) with a p-value of 0.5547 and surgical margins (1 robotic, 2 laparotomy) with a p-value of 0.2065 were similar in both groups and no statistical significance was found.

The median follow up was 28 months in the laparoscopic group in comparison to 53 months for the laparotomy group (p=0.0006). Of the 34 patients, the overall disease free patients were 88% at last follow-up; with 94% in the robotic group and 88% of the laparotomy group disease free at last follow up. The pattern of recurrence in the robotic group included 1 patient with bone metastasis, however, in the laparotomy group 2 had recurrence; 1 at the vaginal cuff and 1 at the pelvic side wall. These findings were not found to be statistically significant.

Conclusion:

Robotic surgery is well established as a safe and feasible treatment of early cervical cancer. In this study, survival outcome is equivalent to open surgery with the added advantage of shorter hospital stay, decreased blood loss and decreased post operative complications. Robotic surgery offers significant improvement in patients’ recovery and morbidity as well as quality
LAPAROSCOPIC PARAAORTIC INFRARENAL LYMPHADENECTOMY: ANATOMIC ANOMALIES FOUND IN OUR SERIES OF CASES AT THE GYNECOLOGIC ONCOLOGY SECTION, DEPARTMENT OF GYNECOLOGY, HOSPITAL ITALIANO DE BUENOS AIRES

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Objectives:
To describe the anatomic anomalies found in a series of laparoscopic paraaortic lymphadenectomies.

Methods:
We included 110 consecutive patients with gynecologic malignancies who underwent laparoscopic paraaortic infrarenal lymphadenectomy, between June 2007 and May 2014.

Results:
One hundred patients underwent transperitoneal laparoscopic lymphadenectomy. Ten other patients underwent extraperitoneal lymphadenectomy. The dissection began at the aortic bifurcation, and the cephalic limit was the renal vein. Vascular abnormalities were identified in 4 patients, no intraoperative vascular injuries were observed.

Case 1: Inferior polar artery branching from the right common iliac artery, two centimeters below the aortic bifurcation, up to the lower pole of the right kidney.

Case 2: Right and left polar arteries originate from the aorta, two centimeters above the inferior mesenteric artery, with abnormal drainage to both kidneys.

Case 3: The left kidney is located in the left pelvis and the right, on the psoas muscle. The right renal vein can be seen draining from the right kidney directly to the inferior vena cava. An inferior polar artery from the right common iliac artery.

Case 4: The left renal artery emerges from the aorta, two centimeters below the left renal vein, and irrigates the left kidney.

Conclusions:
The incidence of anatomic anomalies in this approach for lymphadenectomy described in the literature is variable, ranging between 2% and 40%. In our experience, they occurred in 3.63% of cases. Although preoperative complementary studies were not always conclusive in our series, it seems important to identify the
site and type of vascular anomalies through diagnostic imaging, in order to help reduce or prevent intraoperative vascular trauma.
O&G RESIDENTS IN BRAZIL WOULD CONSIDER GYNECOLOGIC ONCOLOGY AS A SUBSPECIALTY IF IT WERE OFFICIALLY RECOGNIZED AND DON'T FEEL READY TO PERFORM RADICAL HYSTERECTOMIES

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Improvement of gynecological cancer patients’ outcome when treated by gynecological oncologists is well documented. Training is based on surgical and clinical skills acquired through intensive training in specialized centers. The difference in survival is best documented in advanced ovarian cancer patients but evidence is available to other types of gynecological cancer as cervical cancer. (1-3)

The European Society of Gynaecological Oncology (ESGO) and the Society of Gynecological Oncologists (SGO) have clearly defined standards for certification of training centers and individuals. (2, 4)

There is no standardized certification program in gynecologic oncology in Latin America, exception is Argentina and its local certification program led by the local society (AAGO). In order to understand the perception of O&G residents about the need and potential benefits of an organized certification system in gynecologic oncology we conducted an online survey in Brazil in 2014.

Reply summary:

How much does the official recognition of your decision to pursue a subspecialty?

A lot – 80%    Not really – 20%

If Gynecologic Oncology was a recognized specialty would you consider it?

Yes – 70%    No – 20%

Were you able to perform a Type C2 hysterectomy at the end of your residency?

Yes – 40%    No – 60%

Gynecology and obstetrics residents in Brazil are aware of the importance of training in gynecologic oncology. They often don't pursue it because it lacks certification and consider themselves unable to perform the most common radical surgery for gynecological cancer in their country when leaving their gynecology and obstetrics residency.
CLINICAL ADVANTAGES OF NERVE-SPARING RADICAL HYSSTERECTOMY OF CERVICAL CANCER

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Background:
Radical hysterectomy (RH) is the standard treatment approach for early stage of cervical cancer, nevertheless, it is associated with urinary tract dysfunction and colorectal motility disorder that affect quality of life. RH frequently require several days of Foley catheter use, in order to avoid bladder denervation complications.

Aim:
The objective of the study was to analyze the clinical impact of nerve-sparing technique in radical abdominal hysterectomy.

Methods:
Prospective descriptive study of 25 patients with early stage of cervical cancer, who were operated with nerve sparing technique and radical abdominal hysterectomy, between June of 2010 and January of 2015, in Carlos Van Buren Hospital. In all patients Foley catheter was retired prematurely in postoperative. Urinary catheterization was performed until the post-void residual urine volume was < 100 ml. Clinical variables that were evaluated are: postoperative complications, days of Foley catheter use, the need of bladder catheterization, days of hospital stay and survival rate.

Results:
Mean age was 48 years. The operating time average was 4,5 hours. Hospital stay was in average of 3,5 days. Only 4 patients needed measurement of post-void residual urine volume more than 4 days. Nowadays all patient are alive.

Conclusion:
In all patients was possible to identify and preserve the hypogastric plexus and splanchnic nerve. The results showed shorter hospital stay, which lowers costs and contributes to a quick clinical recovery. It has similar survival rates with RH, but its associated with lower postoperative morbidity and good clinical efficacy for treating patients with early cervical cancer.
DETECTION OF E6-E7 MRNA OF HIGH RISK HUMAN PAPILLOMAVIRUS IN NEGATIVE LYMPH NODES IN PATIENTS WITH CERVICAL CANCER: A POSSIBLE EARLY BIOMARKER OF SUBCLINICAL METASTASIS

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Background:
About 4500 new cases are diagnosed and 2000 deaths take place per year by cervical cancer (CC) in Argentina. Persistent high risk Human Papillomavirus (HPV) infection is necessary for the neoplastic transformation, based on the interference of E6-E7 viral proteins in the control of cell proliferation. Lymph node metastasis defines the adjuvant therapy and the prognosis of the disease.

Objectives:
To investigate the expression of E6-E7 high risk HPV oncogenes, detecting the presence of their mRNA in the lymph nodes of patients with operable CC as an early predictor of subclinical metastasis.

Methods:
Multicentric and prospective trial. There were included 24 patients with operable CC, analyzing samples of the central tumor and at least 2 pelvic lymph nodes. Fresh tissue samples were collected in RNALater, (Invitrogen), and the RNA was extracted using the MiniMag (Biomerieux) system. mRNA of the E6-E7 proteins of the genotypes 16,18,31,33 and 45, was detected through a real time isothermal PCR reaction (NucliSENS EasyQ HPV, Biomerieux).

Results:
HPV was found in all the cases, being the identified genotypes: HPV16 (n=17), HPV18 (n=1), HPV31 (n=2), HPV45 (n=2), HPV59 (n=1) y HPV73 (n=1).

In patients with histologic lymph node metastasis, the viral mRNA was detected, being the same genotype that was found in the primary tumor. In 4 patients with negative lymph nodes, the viral RNA was also detected and coincided with the genotype identified in the primary tumor.

Conclusions:
There was a high correlation between the mRNA E6 and E7 detection and histologic findings. The presence of mRNA indicates the transcription of the viral genome that only occurs in metastatic cells of CC. So, the viral mRNA in the negative lymph nodes could point out an early and pre-histological metastasis. It could imply a new diagnostic tool for monitoring CC patients. It is necessary to recruit more patients to validate these findings. *(Grant from Agencia Nacional de Promoción Científica y Tecnológica, PICT 1259).*
**THE ABDOMINAL RADICAL TRACHELECTOMY SPARING THE UTERINE ARTERIES (A.R.T.-S.U.A) & THE PELVIC AUTONOMIC PLEXUS (P.P.A.P.) IN CERVICAL CANCER (CC): ONCOLOGICAL & FERTILITY OUTCOMES OF THIS NOVEL SURGICAL TECHNIQUE**

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**Objectives:**

**Mat & Meths:**
Technique designed for FIGO stages Ia2, Ib1 CC < 2cm; the >2 and < 3cm, received Platinum based neoadjuvant chemotherapy (NCH). Between 10/04-2/14, 24 pts. were included, by the intention to treat. The oncological outcomes, age, surgical feasibility, radicality measured in the surgical specimen, and compared with an Historical group of C1 RH; histological type; blood loss, uterine blood flow evaluated by color doppler ultrasound; operating time; mean hospitalization time; complications; recurrences; pregnancies and follow up were also analyzed.

**Results:**
The technique was performed in 20/24 cases. Age: 27.1 years (21-32). Five pts. received NCH. Radicality (surgical specimen): No differences were found in radicality with C1 RH. Blood loss: 600 ml. Operating time: 180 minutes. Bladder catheterization: 48 hs. Postmicturition residual volume: < 50 ml. Normal indices of doppler blood flow were found. Mean Hospitalization time: 4 days. Complications: 1 case of dyspareunia + cervical poliposis. 1 case of dysmenorrhea. three pregnancies observed, all of them after NCH. One ended in an abortion at the 3rd month, and the other two underwent an elective cesarean section at 35.5 weeks, obtaining two healthy newborns. No complications and no evidence of disease were observed. Recurrences: 2/24 (8.3%), submitted to chemorradiation (CHRt). Deaths: (2/24-8.3%) DFS & O.S: 91.7%. Follow-up: 66 months (13–120).

**CONCLUSIONS:** The ART-SUA-PPAP was feasible, and oncologically safe. It could be taken into account as treatment for the IA2-Ib1 cervical cancer. Neoadjuvant chemotherapy may has a role in selected patients. A large number of cases series,
are needed to valid these results.
GESTATIONAL TROPHOBLASTIC DISEASE: INCREASE OF INCIDENCE IN CARLOS VAN BUREN HOSPITAL, VALPARAISO - CHILE

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Background:
Gestational trophoblastic disease (GTD) represents an heterogeneous group of disorders that are characterized by an abnormal proliferation of trophoblastic tissue. The reported incidence varies widely in different regions of the world. The incidence of molar pregnancy in Japan (2/1000 pregnancies) is greater than the reported incidence in Europe or North America (0.6–1.1/1000 pregnancies). In Chile the reported incidence of GTD is 1/1000 pregnancies.

Aim:
The objective of the study was to analyze the clinical features of gestational trophoblastic disease treated in a regional chilean center.

Methods:
Retrospective descriptive study of patients who were diagnosed GTD, during the year 2014, in Carlos Van Buren Hospital (Valparaiso - Chile).

Results:
There were 2800 deliveries in 2014. Fourteen GTD were diagnosed: five complete hydatidiform mole, seven partial hydatidiform mole and two choriocarcinoma. The incidence of GTD was 5/1000 pregnancies. The mean age was 29 years (between 16 - 58 years). The most common symptom was vaginal bleeding (71%) during first trimester of pregnancy. The mean value of human chorionic gonadotropin was 200.920 mUI/ml. Eleven of twelve hydatidiform mole were resolved with suction evacuation and curettage. Of the two choriocarcinoma, one patient was treated with multi-agent chemotherapy, and the other died early after diagnosis because of hemorrhagic brain metastases.

Conclusion:
The regional incidence of GTD is higher than the expected in Chile, this could be explained by improved diagnostic techniques. However, national population-based studies should be performed, ideally through a centralized registry to guarantee unbiased data.
MOLECULAR CHARACTERIZATION OF GESTATIONAL TROPHOBLASTIC DISEASE

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Background:
Gestational Trophoblastic Disease (GTD) is a condition that relies on clinical findings. Molecular markers have been described as prognostic factors but none of them are currently used for this purpose. The aim of this study was to evaluate cellular proliferation factors in different entities of GTD and evaluate their usefulness as prognostic factor.

Methods:
Retrospective, single institution analysis of samples from patients with GTD from 2010-2014. Immunohistochemistry assessment was performed. The following markers were assessed: anti-apoptotic protein bcl-2, cell-cycle regulatory protein p21 and cyclin D1, oncogene CD 99.

Results:
17 patients were evaluated. They presented with the following entities: complete mole, partial mole, persistent mole and choriocarcinoma. Complete, partial and persistent mole expressed bcl-2, p21 and cyclin D1, whereas choriocarcinoma did not express any of the markers previously named.

Conclusion:
Management of GTD at any condition is still based on clinical findings. Molecular characteristics did not show any difference among complete, partial and persistent mole. However, choriocarcinoma losses the expression of the molecules previously identified. These findings might reflect a deregulation of the cell cycle among patients with confirmed malignancy compared to patients with complete, partial or persistent mole. Future research may focus on the determination of new molecules.
ROLE OF INDOCYANINE GREEN (ICG) IN SENTINEL NODE MAPPING IN GYNECOLOGIC CANCER: A TIME FOR A NEW STANDARD OF CARE?
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Background:
Sentinel lymph node biopsy has proven safe and feasible in a number of gynecologic cancers. To date the most commonly used tracers are technetium-99 and blue dye and these are associated with a detection rate of up to 80-85%. Fluorescent tracers, such as indocyanine green (ICG) are becoming increasingly more popular when performing sentinel node mapping.

Methods:
We searched in Medline, Pubmed, and BioMed Central using the terms 'indocyanine green", "cervical cancer", "endometrial cancer", and "sentinel lymph node" between 1994 and 2014. We included all English-language articles reporting on the use of ICG in gynecologic cancers.

Results:
A total of 8 articles were identified and met inclusion criteria. A total of 354 patients were reported in the published articles. We also identified 472 patients published in the form of an abstract. This totalled 825 patients. Of these, 701 (84.9%) patients had endometrial cancer and 124 (15.1%) patients had cervical cancer. The majority of patients (97.2%) had a cervical injection. Sentinel node detection rate for cervical injection ranged from 83-100%. The detection rate for the only series evaluating
hysteroscopic injection was 33%.

<table>
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<th>Author(s)</th>
<th>Year</th>
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<th>Technique</th>
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<td>ICG 97%</td>
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<td>172</td>
<td>ICG</td>
<td>Cervical</td>
<td>95%</td>
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Conclusions:
ICG is a novel and safe technique to identify SLN in patients with cervical and endometrial cancer. Sentinel node detection rates are very favourable.
IGCS-0086
Imaging / Staging

LAPAROSCOPIC TREATMENT FOR ISOLATED PARA-AORTIC LYMPH NODE RECURRENCE
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Objectives:
Evaluate the feasibility and efficacy of laparoscopic debulking of para-aortic lymph node recurrence in gynecologic malignancy.

Methods:
A retrospective study where 12 patients with unique and isolated recurrence during follow up, were evaluated and treated in Hospital Italiano of Buenos Aires division Gynecologic Oncology; from January 2010 to December 2014.

We analyzed the average patient age, body mass index (BMI), initial pathology, and primary treatment. Then we evaluated perioperative outcomes: type of surgery and technical approach, complications (intra and postoperative), conversion to laparotomy, time of surgery, hospital stay, number of lymph nodes resected and node size was analyzed.

Results:
We treated 12 patients with different gynecological malignancies, among which stand out; cervical, ovarian, endometrial and breast cancer. The median hospital stay was 36 hrs; the median time of surgery was 130 hrs; the average size of the lymph nodes was 2.91 cm (Max 5 cm and min 1.2 cm); 0% conversion to laparotomy

Conclusions:
We consider that the secondary cytoreduction is feasible in selected patients with few complications. While there are multiples technical approach (transabdominal, laparoscopic transperitoneal or retroperitoneal), in our center we have a vast experience in the laparoscopic technique, which is why all of our patients have had a minimally invasive surgery. Randomized clinical studies are needed to define the best therapeutic strategy for these patients.
ASSESSMENT OF POSTOPERATIVE MORBIDITY RISK AFTER HYSTERECTOMY USING THE SURGICAL APGAR SCORE
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Objectives:
To apply the ten point surgical APGAR score in women who underwent hysterectomy to assess its effectiveness in estimating post-operative risk.

Methods:
Women who underwent a hysterectomy from July 1, 2013 to June 30, 2014. Medical records were reviewed for demographics, comorbid conditions, body mass index, intra-operative body temperature, time between antibiotic administration, and post-operative complications. The ten point score was calculated based on the estimated blood loss, lowest heart rate, and the lowest mean arterial pressure. Post-operative complications were defined as transfusion of 2 or more units of packed red blood cells, deep vein thrombosis, sepsis, bleeding complications, surgical site infections or prolonged intubation post-surgery. Chi-square, Fisher’s exact, t-test and logistic regression were performed.

Results:
A total of 150 cases were performed – 89 abdominally and 61 minimally invasive. Mean age was 54.3 and mean BMI 32.8. Half of the cases had a final diagnosis of a malignancy. Post-operative complications were associated with a surgical apgar score ≤5 (p=0.001) and abdominal hysterectomy (p=0.004). Comorbid conditions, malignancy, BMI, ASA class, performance status, time of antibiotic administration and hypothermia intra-operatively were not associated with complications or a lower surgical Apgar score.

Conclusions:
A lower surgical Apgar score ≤5 strongly predicts post-operative morbidity and complications in hysterectomies. This intra-operative scoring system provides a method of determining the level and extent of care needed to reduce post-operative complications and to better mitigate risks for patient’s recovery and quality of life.
THE RELATIONSHIP BETWEEN SELF-EFFICACY AND ADHERENCE TO PAP TEST IN A GROUP OF CHILEAN WOMEN
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Background:
According to Bandura’s social cognitive theory, self-efficacy is one’s confidence in being able to exert personal control.

Aim:
To analyze the relationship between adherence to Pap smear and self-efficacy in a group of Chilean women.

Methods:
Quantitative study in 706 Chilean women. The adherence was measured as positive if the woman have had a Pap test in the last three years, and Negative if the woman have had the Pap test more than three years or never. The Self-efficacy was measure with SES-PSSP questionnaire. IRB approved this study.

Results:
78% of the women had a positive adherence to Pap test. The probability to take the Pap Test is different between both groups, the women who had positive adherence has a highest probability to take the Pap test in different situations that the questionnaire ask to them; the one and only concern in where both group were similar (no statistics difference) was the question about “the need that the children were care by others”.

Discussion:
The level of woman’s self-efficacy may vary for different situations, but in this study the women with positive adherence had the same level in different questions, and it was different to the negative adherence group. The only topic that was similar level between both groups was the related to the care of children, showing that the care of others is an important concern to the Hispanic women and Chilean women also. Nursing must be to consider this aspect when the educational intervention will be proposed.
Cervical cancer is the third most common cancer among Brazilian women.\(^{(1, 2)}\) In developing countries such as Brazil and most of Latin America, advanced stages are more frequent than in the developed world (34% of newly diagnosed cases in stages III and IV), while 41% diagnosed in early stages. Therefore most patients are treated with a combination of chemo, radiotherapy and maybe also radical surgery (Mostly types C1 or C2 radical hysterectomy).\(^{(3, 4)}\)

Adjuvant therapy can cause several long-term physical consequences. Chemotherapy can cause fatigue or severely impair ovarian function. Radiotherapy, either external or brachytherapy can cause vaginal sequels by damaging nerves and blood vessels.\(^{(5)}\) However, the effect of surgery alone on sexual function in these patients is still controversial.\(^{(6)}\)

Systematic reviews on the subject of quality of life and sexual function in cervical cancer patients include the use of non-validated questionnaires.\(^{(5-8)}\) There are four questionnaires which have previously been validated in patients with cervical cancer, one disease-specific questionnaire and three dimension-specific questionnaires:\(^{(6)}\)

1. The European Organization for Research and Treatment of Cancer Quality-of-Life Questionnaire-Cervix Module 24 (EORTC QLQ-CX24)\(^{(6, 9)}\)
2. The Female Sexual Function Index (FSFI)\(^{(6, 10)}\)
3. The Leiden Questionnaire\(^{(6, 11)}\)\(^{(15, 29)}\)
4. The Sexual Function-Vaginal Changes Questionnaire (SVQ)\(^{(6, 12)}\)\(^{(15, 30)}\)

We performed a literature search in six online databases and search tools and retrieved only 6 prospective studies which used validated questionnaires. Therefore a methodology assessment is imperative when interpreting results from studies on quality of life of cervical cancer survivals.
LIFETIME RISK OF OVARIAN CANCER BASED ON ENDOMETRIOSIS AND OTHER RISK FACTORS

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Background and aims:
Ovarian cancer is rare but deadly. We identified combinations of known risk/protective factors that put women at low and high risk for ovarian cancer in order to create risk strata.

Design:
Pooled analysis of case-control studies from the Ovarian Cancer Association Consortium.

Methods:
We applied published risk estimates for risk/protective factors to multiplicative models to calculate every possible combination. To convert to absolute risks we divided each combination-specific relative risk by the frequency-weighted average of all the combination-specific relative risks and scaled to a weighted average of unity.

Results:
214 combinations of risk/protective factors were observed among 4497 cases and 4497 controls. As compared to a U.S. registry average lifetime risk of 1.37%, lifetime risks here ranged from 0.35% to 8.78%. Women in the lowest five categories (<0.5% lifetime risk) all used OCs 5+ years, bore children, and had no family history and no endometriosis. Women with the highest lifetime risk (> 5%) all had either a family history or endometriosis; no tubal ligation; never used OCs (7/8 categories). Genetic risk profiles were diverse. Comparing lifetime risks showed, for example, a woman at moderate risk (4.3%) because of no tubal ligation and nulliparity (but no family history and no endometriosis) would reduce her risk to 1.7% if she used OCs for 5+ years.

Conclusion:
A >20-fold differential in risk resulted from various risk/protective combinations. Although relatively uncommon, some women had substantial lifetime risk based on
reported risk factors and lack of behaviorally modifiable choices.

Dr. Ness is an expert witness for plaintiffs in cases involving the use of talc in relation to ovarian cancer.

**IGCS-0015**  
**Ovarian Cancer**

**DOES TALC EXPOSURE CAUSE OVARIAN CANCER?**  
**R. Ness**  
Epidemiology, University of Texas School of Public Health, Houston, USA

**Background and Aims:**  
Controversy surrounds the question of whether talc use causes ovarian cancer.

**Design:**  
Formal systematic analysis of talc use and ovarian cancer.

**Methods:**  
All accumulated epidemiologic evidence (23 case-control studies, 5 meta-analyses, and 3 analyses of a single cohort) and basic science studies were reviewed and graded for quality. Data were considered overall and by histologic subtype. Attributable Risk estimates were calculated. Factors favoring causality were the well-accepted Hill’s criteria.

**Results:**  
Talc use increased ovarian cancer risk by 30-60% in almost all well-designed studies. The Attributable Risk was 29%, meaning that elimination of talc use could protect more than one quarter or more of women who develop ovarian cancer. Risk elevations were found consistently among good case-control studies, 2 of 3 cohort analyses, and all meta-analyses/pooled analyses. Well-designed studies that considered dose-response by both duration and frequency all found higher risk among women exposed to more applications. A plausible biologic mechanism is inflammation, known to cause other epithelial cancers. The talc association is more specific to serous ovarian cancer. Systematic bias is excluded because talc use is a durable behavior unlikely to be subject to recall bias; good case-control studies were all population-based or cohorts averting selection bias; and multiple adjustment for other risk factors limited confounding.

**Conclusion:**  
Hill’s tenets suggest that talc use causes ovarian cancer. Several, but not all, baby powder manufacturers have already replaced talc with corn starch.
**IGCS-0018**  
**Ovarian Cancer**  

**SURGICAL STAGING OF OVARIAN CANCER (I FIGO STAGE)**  
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In stage I epithelial ovarian cancer the surgery is the primary treatment approach. The purpose of the surgery is accurate staging process. A major role in this staging is retroperitoneal lymphadenectomy (pelvic and paraaortic). After proper staging, patients are indicated for adjuvant chemotherapy, combined (chemotherapy and target-chemotherapy) chemotherapy or fertility-sparing surgery.

**Objective:**  
To present the importance of staging (pelvic and paraaortic lymph node dissection) for the treatment and prognosis of patients with 1st stage ovarian cancer.

**Material and methods:**  
Between 2006-2012, 40 patients were diagnosed in 1st stage ovarian cancer, which were surgically treated. The latest achievements of the science - randomized studies and own clinical material (analysis of medical history) and a technique of paraaortic lymph node dissection to the level of the left renal vein were presented.

**Results:**  
In 25 patients (62.5%) a complete surgical staging was performed. In 3 of these 25 patients (12%) are established lymph node metastases were established, i.e. staged as IIIC FIGO stage.

**Conclusion:**  
In early stage ovarian cancer paraaortic lymph node dissection is a required step of proper staging, which determines the treatment and prognosis of these patients.
Ovarian Cancer

ADVANCED STAGE OF EPITHELIAL OVARIAN CANCER (II-IV FIGO STAGE). 
THE ROLE OF LYMPH NODE DISSECTION
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The surgery has a leading role in the primary treatment of advanced ovarian cancer (II-IV stage) (AOC). Efforts in surgery is aimed at "optimal" cytoreduction (without visible tumor). Some patients primary are indicated for neoadjuvant chemotherapy and secondary cytoreductive surgery. Retroperitoneal LN are common place for metastases (especially paraaortic lymph nodes), the risk of metastases increases with the stage.

Objective:
To demonstrate the role and importance of lymph node dissection (LND) to achieve optimal cytoreduction in AOC.

Material and methods:
Between 2006-2012, 52 patients - 6 (II stage), 44 (II stage) and 2 (IV stage) AOC which have been operated on, are included in the study. A technique of pelvic and paraaortic LND in bulky, massive lymph node metastases as a part of optimal cytoreduction has been presented. This group doesn't include cases with borderline malignancy, nonepithelial tumors, secondary (metastatic) ovarian tumors and synchronous tumors, as well as patients with suboptimal cytoreduction.

Results:
For II stage in 6/6 (100%) patients LND was performed. In 2/6 (33%) microscopically paraaortic lymph node metastases were identified. For III stage in 32/44 (73%) patients LND was carried on. In 17/32 (53.1%) lymph node metastases (paraaortic / pelvic and paraaortic) were established. In 12/17 (71%) metastases are massive (lymph packages). In 5/17 (29%) microscopic metastases were found.

For IV stage - in 1/2 patients lymph node dissection was performed and result is microscopic lymph node metastases.

Conclusion:
Paraaortic LND provides an exact staging of stage II (33% of cases are substaged); removes residual microscopic disease in stage III (in 29% occult metastases) and it is related to optimal cytoreduction for stage III (in 71% there were bulky, massive metastases).
IGCS-0038
06. Ovarian Cancer

NHE1 PROMOTE CELL PROLIFERATION IN OVARIAN CANCER: A ROLE OF HYPOXIA-INDUCIBLE FACTORS.
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¹Cellular and Molecular Physiology Laboratory (CMPL), Division of Obstetrics and Gynaecology School of Medicine Faculty of Medicine Pontificia Universidad Católica de Chile Santiago 8330024 Chile, Santiago, Chile
²Department of Obstetrics and Gynecology, Faculty of Medicine Pontificia Universidad Católica de Chile Santiago Chile, Santiago, Chile
³Biomedical Department, Faculty of Health Sciences Universidad de Antofagasta Antofagasta Chile, Santiago, Chile

Background:
Ovarian cancer is a highly lethal disease. Tumour cells must adapt to oxygen (O₂) levels and excessive production of H⁺ to proliferate. Hypoxia-inducible factors (HIFs) and Na⁺/H⁺ exchanger isoform 1 (NHE1) plays a major role in low O₂ adaptation, pH control and promoting cell proliferation.

Aim:
To evaluate the role of NHE1 in human ovarian cancer cell proliferation in hypoxia.

Methods:
Ovarian cells lines HOSE (normal), A2780 (tumour) and human primary cancer cells from ascites (hCC) were exposed (0-48 hours) to 20% O₂ (normoxia) or 10% O₂ (permissive O₂). Cell proliferation was assessed by cell counting (haemocytometer). NHE1 expression was assessed by RT-qPCR, western blot, and immunofluorescence. NHE1-activity was estimated by pH recovery rate (dpHi/dt) (BCECF-AM) in a gas controlled-fluorimeter.

Results:
NHE1 was detected in human ovarian cancer tumour and stroma and in promigratory-structures in ovarian cancer cells. Inhibition of NHE1 by zoniporide (100 nM), but not concanamycin A (V-type ATPase inhibitor) or Schering 28080 (H⁺/K⁺ ATPase inhibitor), reduces dpHi/dt in HOSE (~50%), hCC (~50%), and A2780 (~90%). Additionally, NHE1-knockdown reduces dpHi/dt (~65%) and zoniporide reduces (~60%) migration in A2780 cells. NHE1 protein abundance and mRNA expression were increased, and zoniporide-inhibition of NHE1 reduced cell proliferation under 10% O₂. NHE1 dpHi/dt at 10% O₂ was increased at 3-6 hours remaining unaltered for 18 hours incubation. HIF2α-knockdown reduces NHE1 activity and expression in A2780 cells.
Conclusions:
NHE1 activity is pro-proliferative under permissive O$_2$ requiring HIF2α expression in human ovarian cancer cells.

Acknowledgments
FONDECYT 3140516, 1110977, 11110059, 3130583.
DIFFERENTIALLY EXPRESSED MiRNAs AND THEIR SURVIVAL PREDICTION IN THE HIGH GRADE SEROUS AND CLEAR CELL OVARIAN CARCINOMA

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The goal of this study was to identify a unique miRNA pattern and key miRNAs that could predict the progress and survival in high-grade serous ovarian carcinoma (HGSC) and clear cell ovarian carcinoma (CCC).

To identify a unique miRNA pattern associated with HGSC and CCC, a miRNA microarray was performed using Chinese tumor bank specimens of patients with HGSC or CCC in a retrospective analysis. The differential expressed miRNAs were further validated using qRT-PCR. Kaplan-Meier analysis was performed to analyze the correlation between miRNAs expression and patients prognosis. The validated miRNAs were finally examined in another cohort of normal ovarian tissues, HGSC, LGSC and CCC specimens by qRT-PCR and in situ hybridization.

The results showed that of the 768 miRNAs analyzed in the microarray, 33 and 50 miRNAs were significantly either up- or down-regulated, with at least a 2-fold difference, in HGSC compared to CCC. The quantitative analysis showed that miR-510 and miR-129-3p were down-regulated, and miR-483-5p and miR-449a were up-regulated in CCC compared to HGSC, which was consistent with the microarray results. Kaplan-Meier analysis showed low miR-510 and miR-129-3p were associated with advanced FIGO stage and status of lymphatic metastasis, which were further confirmed by the patients, who were followed up, with the poorer overall survival (P<0.05).

Our results suggest that different subtypes of EOC have specified miRNAs signatures., MiR-510 and miR-129-3p may be considered as the potential novel candidate clinical biomarkers for predicting EOC outcome.
Background and aims:
Pelvic lymphadenectomy is essential element of surgical treatment of gynecologic malignancies. However, it can induce asymptomatic and symptomatic pelvic lymphoceles (LC) in a considerable percentage of patients. Therapy of symptomatic LC may cause additional morbidity.

Objectives of this study were to evaluate feasibility and safety of Tachocomb® (fibrin sealant hemostatic patch, in English-language countries known as TachoSil) usage, the incidence of LC in advanced ovarian cancer patients with and without Tachocomb® usage.

Methods:
A total sample size of 60 advanced ovarian cancer patients (30 in each treatment group) was evaluated. Radical histerectomy with omentectomy and pelvis lymphadenectomy (LE) was performed at the Department of Gynecology at Almaty Oncology Center (Kazakhstan, Almaty city). Application of Tachocomb® and placement of routine pelvic bilateral drainage after LE were used in 30 patients (Group 1). Case-control comparison was done in 30 patients (Group 2) with bilateral drainage after complete LE without Tachocomb® use. Detection of LC was done during oncologic follow-up by sonography on 5th, 7th, 14th, and 20th postoperative days.

Results:
Lower volume and duration of lympharea was shown in Group 1. LC was detected in 2 patients of Group 1 (6%) and in 10 patients of Group 2 (30%), with statistically significant difference.

Percutaneous drainage was used only in 1 case (Group 2).

Conclusions:
Intraoperative Tachocomb® usage after pelvic lymphadenectomy is feasible, safe, can reduce duration of hospital stay and potentially decrease rate of symptomatic LC in patients with gynecologic malignancies.
IFOSFAMIDUM AS PALLIATIVE TREATMENT FOR ADVANCED OVARIAN CANCER

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Background and Aims:
The aim our study is to determine safety, feasibility and efficacy of ifosfamidum treatment in patients with persistent or recurrent ovarian cancer. These patients usually receive multiple chemotherapy courses and the resistance is steadily increasing. Therapy possibilities are limited in Latvia due to the insufficient compensation of the medicaments. Therefore it is crucial to select out-dated medicaments which would be effective in the cases of heavy pre-treated patients.

Methods:
Eligible patients included persistent or recurrent epithelial ovarian cancer with 2-5 prior regimens and PS 0-2. All 47 patients were retrospectively reviewed from 2010 – 2013 from hospital records. Response and toxicity were collected.

Results:
42 patients were evaluable. The clinical benefit rate (PR and SD) at 4 months was 57%, but there were no objective responses. All patients had stable disease. The most frequent treatment-related grade ¾ adverse events included neutropenia (60%), anaemia(19%), thrombocytopenia (15%) and fatigue (65%). No drug related cardiotoxicity/neurotoxicity was observed. There were no treatment-related deaths.

Conclusion:
Ifosphamidum administration is the safe and feasible therapeutic option for persistent and recurrent ovarian carcinoma, particularly in countries without trabectin and doxil reimbursement. Single agent ifosfamidum offers a promising therapeutic option in heavily pre-treated ovarian cancer.
IGCS-0065
Ovarian Cancer

CAN WE IMPROVE DETECTION OF BORDERLINE OVARIAN TUMORS?
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2Obstetrics and Gynecology Division of Gynecologic Oncology, New York Medical College, New York, USA
3Radiology, New York Medical College, New York, USA

Purpose:
To evaluate the utility of clinical characteristics and frozen section in diagnosing borderline ovarian tumors (BOT).

Methods:
After IRB approval, medical records and digital images for patients with frozen or final diagnosis of BOT were retrospectively reviewed from 2010 to 2014. A dedicated gynecologic pathologist reviewed all specimens.

Results:
Findings and comparison between mucinous borderline ovarian tumor (MBOT), serous borderline ovarian tumor (SBOT), and malignancy are summarized in Table 1 for all 39 patients.

Sixty-two percent of patients with MBOT had pelvic pain, whereas 71.4% of patients with SBOT presented with abnormal bleeding. Twenty patients underwent CT, 8 had ultrasound, and 6 had MRI. On imaging, none had lymphadenopathy. Laterality and tumor size were concordant to final pathology.

Overall positive predictive value (PPV) of frozen section was 79.2%. For MBOT, PPV was 69.3%, and 90.9% for SBOT. In 11 MBOT patients with frozen section, there were 2 discordant cases. In SBOT patients, 12 had frozen pathology with 2 discordant cases. Frozen specimen was benign in one discordant case and malignant in the other for both groups. Five patients with malignancy had BOT on frozen section: 4 MBOT and 1 SBOT.

Conclusions:
Pelvic pain and large tumor size may suggest BOT. Cystic tumors larger than 5 centimeters without radiographic lymphadenopathy may exclude malignancy. Frozen section is not as precise in diagnosing MBOT compared to SBOT. Future studies of
pre-operative nomograms could be useful in counseling women suspected of BOT.

Table 1: Summary of findings and comparison by final pathology

<table>
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<tr>
<th></th>
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<th>MBO1T</th>
<th>SBOT</th>
<th>Malignancy</th>
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<tr>
<td>Patients (n)</td>
<td>39</td>
<td>16</td>
<td>16</td>
<td>5</td>
</tr>
<tr>
<td></td>
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<td>Range</td>
<td>Median</td>
<td>Range</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46</td>
<td>17-72</td>
<td>45</td>
<td>18-69</td>
</tr>
<tr>
<td>CA 125 (U/mL)</td>
<td>47.8</td>
<td>5.6-4499.2</td>
<td>38.6</td>
<td>6.3-3857</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>Range</td>
<td>Median</td>
<td>Range</td>
</tr>
<tr>
<td>Presentation</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Pelvic Pain</td>
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<td>41</td>
<td>10</td>
<td>62.5</td>
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<tr>
<td>Vaginal Bleeding</td>
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<td>17.9</td>
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<td>0</td>
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<tr>
<td>Asymptomatic</td>
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<td>17.9</td>
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<tr>
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<td>2</td>
<td>12.5</td>
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<tr>
<td>Size &gt; 5 cm</td>
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<td>90.1</td>
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<tr>
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</tr>
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<td>Frozen section</td>
<td>29</td>
<td>74.4</td>
<td>11</td>
<td>68.8</td>
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Background:
Brain metastases in patients with epithelial ovarian cancer (EOC) are an uncommon finding and associated with poor prognosis. The aim of this study was to review the clinical characteristics of patients with brain metastases and molecular findings in the primary tissue.

Methods:
Retrospective, single institution review of the patients who were histological confirmed with EOC between 2007 and 2014.

Results:
Four patients were identified. All of them had High Grade Serous histology. Mean age at diagnosis was 49 years (39-72). Median time from diagnosis of the disease to diagnosis of brain metastases was 39months (14–66), median survival 45m (17–77) and median time from diagnosis of brain metastases to death/last follow up 5.5 months (3–11). Three patients had disseminated metastatic disease at the time of the diagnosis of brain metastases. Two presented multiple metastases in the brain. One patient received palliative radiotherapy and two patients with single metastases underwent a surgical procedure; one of these received whole external brain radiotherapy after surgery. One patient is still alive with evidence of recurrent brain disease only. From a histological point of view, all samples had strong expression of beta-catenin at the level of the membrane.

Conclusions:
Patients with EOC and brain metastases have a poor outcome. However, single brain metastases and no evidence of disease elsewhere may have better prognosis. Although the presence of beta-catenin has not been associated with brain metastases, its expression has demonstrated a poor prognosis. Multi institutional collaboration and prospective data are needed.
Objective: To evaluate demographic, clinopathologic characteristics, surgery staging and follow up for patients with borderline tumors of the ovary (BOT)

Methods: We performed a retrospective evaluation of the borderline tumor of the ovary between 1996 and 2013. Hospital Dr Sotero del Rio, Santiago de Chile.

Results: We analyzed 141 patients. The median age was 43 years (16-83). Diagnosis was done for abdominal pain in 64% and as ultrasound finding in 26% of patients. Fifty-four patients had fertility sparing surgery with 10 consecutives pregnancies. Histology were serous in 83 (59%), mucinous 42 (29%), seromucinous 4 (3%) and cystoadenofibroma 3 (2%). Bilateral disease occurred in 34 patients. We performed 19 complete surgical staging, 23 appendectomy with normal histology. Stage I were 121 (86%), stage II four (3%) and 12 (9%). Agreement between frozen section diagnosis and definitive histology was 67%. The sensitivity was 71%, positive predictive value (PPV) was 92%. For serous BOT the agreement between frozen section and final histology was 97%. Recurrence were 10 all in conservative surgery. The median follow up was 40 month (12 – 157), two patients died for other pathology, five year survival rate was 100%.

Conclusion: The BOT had an excellent prognosis, fertility sparing surgery is feasible but with strict follow up because of the recurrence increase in this group. Surgical staging with lymphadenectomy and appendectomy not influence in survival. Intraoperative frozen section diagnosis of borderline ovarian tumor has low sensitivity but an acceptable PPV. Serous BOT have and excellent correlation with final histology.
Introduction:
Ovarian, fallopian tube and primary peritoneal cancer are the most lethal of all gynecologic malignancies, with cure rates about 30% for advanced disease, despite improvements in surgical technique and chemotherapy. Numerous studies have demonstrated a survival benefit for patients who undergo optimal primary debulking surgery.

We present our fourteen year experience in the treatment of advanced ovarian, fallopian tube and primary peritoneal cancer.

Methods:
A retrospective analysis of the all advanced ovarian, fallopian tube and primary peritoneal cancer treated at our institution during the last fourteen years.

Results:
A total of 148 patients were treated between January 2000 and May 2014.

The median of age was 56 for the whole cohort. Seventy one percent of cases were stage IIIC and 63% of those patients who underwent surgery had residual disease less than 5 mm. at the end of surgery.

Overall survival for patients with less than 5mm of residual disease after debulking surgery was 70 months and 20 months only for patients with residual disease of 1cm. or more.

Of all variables explored with univariate analysis; residual disease, FIGO stage, age at diagnosis, use of taxanes as first line, drop in 10 times of CA-125 post-op level with respect to that measured before surgery, and use of ultraradical surgery were independent variables for overall survival.

In multivariate analysis, only residual disease after surgery, age at diagnosis, and FIGO stage were independent variables.
Psammocarcinoma is a rare variant of serous ovarian carcinoma, associated with favorable prognosis.

Materials:
In October, 2004, a 44y woman was referred to our Unit with an abdominal pelvic mass and elevated CA 125. Ultrasound and CT scan showed a preuterine tumor 95 x 49 x 47 mm. CA125: 62.

The patient underwent laparotomy: implants involving pelvic peritoneum, omentum, bladder serosa, uterine serosa and cul-de-sac. Both ovaries were macroscopically normal. Total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic lymphadenectomy and resection of the vesicouterine mass were performed. Residual disease was > 1 cm. Pathology: bilateral ovarian Psammocarcinoma G2 with positive peritoneal implants. Lymph nodes were positive (6/9). Peritoneal cytology was negative. FIGO IIIC (1988).

First line chemotherapy (6 courses with Paclitaxel and Carboplatine) was performed between October 2004 and February 2005 with complete response. In May 2005, second look laparotomy showed peritoneal implants in cul-de-sac and appendix serosa. Complete resection was achieved. Pathology: Psammocarcinoma. The patient was considered for radiotherapy (3000 cgy in pelvis + 200 cgy boost) between August and September 2005.

Results:
Follow up was negative until December 2014 when she referred diarrhea. CT scan and MRI revealed a 7 cm complex mass next to rectosigma. CA 125: 71. CA 19.9: 11.3. Colonoscopy showed an extrinsic compression of the rectum. A laparotomic anterior resection of rectosigma with transverse colostomy was performed. Pathology: psammocarcinoma.

Conclusion:
Despite Psammocarcinoma of the ovary and peritoneum is a good prognosis disease, a careful follow up is necessary since long term recurrence have been described.
LEPTIN PROMOTES A MORE AGGRESSIVE BEHAVIOR OF OVARIAN CANCER CELLS: A POTENTIAL EXPLANATION FOR A WORSE PROGNOSIS IN OBESE OVARIAN CANCER PATIENTS

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Obesity is a chronic inflammatory condition linked to cancer risk. However, the evidence linking obesity with ovarian cancer remains controversial. Leptin is expressed at higher serum levels in overweight women and is known to stimulate cell migration and invasion in several epithelial cancers. Here, we explored the clinical impact of overweight in cancer prognosis, and the leptin’s effects on the metastatic potential of ovarian cancer cells. We assessed the clinical outcome (progression free and overall survival) in a cohort of 70 patients with stage III-IV epithelial ovarian cancer (33 normal and 37 overweight) and further validated with an external cohort from TGCA database (high versus normal mRNA leptin/OB-Rb levels). We explored serum and ascites leptin levels and the OB-Rb expression in samples from our cohort. OB-Rb is higher expressed in ascites and metastasis than in primary tumors. Progression-free and overall survivals were significantly decreased in overweight patients. Serum and ascites leptin levels were significantly higher in those overweight patients experiencing worse survival. Similarly, a worse overall survival was found in patients expressing higher leptin/OB-Rb mRNA levels. Leptin exposure increased ovarian cancer cell migration and invasion through leptin receptor-mediated activation of downstream canonical signalling pathways such as MAPK and AKT. Therefore, our findings demonstrate that leptin stimulated cell migration and invasion of ovarian cancer cells, offering a potential explanation for a worse prognosis, particularly among obese women. (research supported by fondecyt 1120292, 1080163, 3140335).
MOLECULAR FINGERPRINTS OF MIXED ENDOMETRIOID AND SEROUS ADENOCARCINOMA OF THE ENDOMETRIUM
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Background:
The molecular biology and cellular origins of mixed type endometrial carcinomas (MT-ECs) are poorly understood, and 10% or less of Type II component may confer poorer prognoses.

Methods:
We studied 10 cases of MT-ECs (endometrioid and serous components), 5 pure low-grade endometrioid adenocarcinoma (EAC) and 5 pure uterine serous carcinoma (USC). Each of endometrioid and serous components of the 10 MT-EC were macrodissected and compared to the expression of 60 candidate genes to profiles from 5 pure USC and 5 pure low-grade EAC.

Results:
We found that four genes were differentially expressed when MT-ECs were compared to pure low-grade EAC: CDKN2A (P=0.006), H19 (P=0.010), HOMER2 (P=0.009) and TNNT1 (P=0.006). Also we found that even though MT-ECs closely resembled the molecular profiles of pure USC, they showed lower expression of PAX8 compared to all pure cases combined (P=0.035).

Conclusion:
Our data suggest that MT-EC exhibits the closest molecular and epidemiological similarities to pure USC and supports clinical observations that suggest patients with MT-EC should receive similar treatment as patients with pure serous carcinoma and MT-EC seemed to have novel specific markers that could be of diagnostic utility and might be a potential targeted therapy in the future.
IGCS-0060
Uterine Cancer, including Sarcoma

UNDIFFERENTIATED ENDOMETRIAL CANCER, A DIFFERENT ENTITY WITH AN AGGRESSIVE BEHAVIOR

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Background:
Undifferentiated endometrial cancer is a relatively new entity with limited information on its clinical behavior. The goal of this study is to review the experience of a single institution in the management of this disease.

Methods:
Using the Juravinski Hospital computerized medical database that contains the pathologic information for all cancer cases treated at our institution, we identified all patients with undifferentiated endometrial cancer diagnosed from January 2005 to December 2012. Clinical information was collected using chart review.

Results:
We identified 22 patients with the diagnosis of undifferentiated endometrial cancer. Medium age was 65 years. Obesity was common, with medium body mass index of 30. Slightly over half (12/22) were diagnosed at stage III or IV. Common metastatic sites were nodal (9/12 patients), hematogenous (6) and intraperitoneal (6). Just 4/12 patients were fit enough to undergo treatment for metastatic disease. None responded to platinum based chemotherapy given as first line treatment or to Doxorubicin as second line treatment, and in fact developed rapidly progressive disease. External beam radiation was used in 2 patients with metastatic disease: one had stable disease within the radiation fields region but developed distant disease within 2 months, the second patient had progressive disease within the radiation fields. Overall survival was 14 months for all patients, and 6 months for patients with stage 3 or 4 disease.

Conclusions:
Undifferentiated endometrial cancer is an aggressive disease with poor response to standard treatments. Further studies are needed in order to improve these patients’ prognosis.
IGCS-0081
Uterine Cancer, including Sarcoma

EARLY STAGE ENDOMETRIAL CANCER: LAPAROSCOPY VS LAPAROTOMY
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Endometrial carcinoma is the 4th most common cancer in females. Surgery (hysterectomy and bilateral salpingo-oophorectomy) is the standard treatment for endometrial cancer clinically confined to the uterus. The traditional surgical staging is laparotomic.

Methods:
Retrospective study. Patients with endometrioid endometrial carcinoma treated (by the same surgical team) in our Unit between January, 2009 and December, 2014. Postoperative outcome and overall survival (OS) were analyzed.

Results:
25 patients underwent to surgery, 15 patients laparoscopically and 10 patients were submitted to traditional laparotomic technique. 4 patients required conversion to laparotomy.

OS was 90.9 % for the laparoscopic group and 92.8 % for the laparotomic one.

Operative time was longer in the laparoscopic group but resulted in fewer perioperative complications, lower blood loss and shorter hospital stays.

Conclusions:
We found no difference in OS between both groups but complications were lower in laparoscopic group.
Unopposed estrogen is known to be associated with an increased risk of endometrial hyperplasia and carcinoma, therefore progesterin is added to prevent this complication. Pharmaceutical progestins, when used in appropriate dose, are very effective. We present two cases of postmenopausal women with an excessive plasma concentration of estradiol using “bioidentical” estradiol gel in custom-compounded HRT preparations without adequate progestin protection.

A 63-years old non-obese woman took oral estradiol 1 mg and norethindrone acetate 0.5 mg daily 6 years, until April 2010. At her last yearly medical check-up in February 2010 the vaginal ultrasonic scan was normal, and the serum estradiol level was 0.12 nmol/L. In December 2012, she visited outpatient clinic. During the last 28 mounts she used 2% compounded topical estradiol gel at a daily dose of “push the pump once” and 6% compounded topical progesterone gel at the “same” daily dose. An ultrasonic scan revealed a thickened endometrial lining 14 mm. The serum estradiol level was 2.87 nmol/L, in a level of controlled ovarian hyperstimulation. She was investigated by diagnostic hysteroscopy and curettage. The tissue diagnosis was atypical endometrial hyperplasia.

A 60-years old obese woman (BMI 26) used “bioidentical” HRT as topical creams containing estradiol, progesterone and testosterone (doses unknown) from February 2011. The creams were posted to her by mail. In October 2013 she visited the outpatient clinic with mild vaginal discharge that lasted 2 months. An ultrasonic scan showed that the endometrial thickness was 22 mm. Diagnostic curettage confirmed a diagnosis of atypical endometrial hyperplasia.
THE SIGNIFICANCE OF PRE-OPERATIVE ENDOMETRIAL SAMPLING IN GRADE 1, LOW RISK ENDOMETRIAL CANCERS

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Background:
To examine (1) the concordance between pre-operative endometrial sampling, frozen section and final pathology in the diagnosis of grade 1 endometrial cancer and (2) whether prolonged time to surgery will result in worsening disease.

Methods:
Pathology and clinical data from women who had surgery from 2010-2014 for grade 1 endometrial cancer on pre-operative, frozen, or final pathology were obtained.

Results:
96 women met inclusion criteria; 90 were identified with grade 1 (G1) endometrial cancer. 92 had pre-operative sampling: 40 with endometrial biopsy (emb), 48 dilation and curettage (D&C), and 4 unknown. 74 patients had frozen section. Figure 1 shows the concordance between D&C versus emb and final diagnosis and proportion of stage 1A disease over time.

Figure 2 illustrates the agreement between pre-operative testing, frozen section and final pathology. D&C specimens were concordant with frozen and final pathology in 61.1% of cases, and emb in 62.5%.

Pre-operative testing over-diagnosed grade 2 (G2) cancer in 10 cases and under-diagnosed complex atypical hyperplasia on 9 cases of G1. Two cases were upgraded from G1 to G2. Frozen section alone upgraded to G2 in two cases where final pathology showed G1.

Conclusions: Endometrial biopsy and D&C are equivalent in diagnosing grade 1 endometrial cancer. Frozen section did not contribute to significant upgrading of specimens from pre-operative evaluation. Prolonged time from sampling until surgery did not result in higher grade or
Figure 1: Concordance and distribution of stage over time

Figure 2: Overall agreement between pre-operative sampling, frozen section, and final pathology
ROBOTIC SURGERY INCREASES PATIENT’S ACCESS TO MINIMALLY INVASIVE SURGERY FOR HYSTERECTOMIES

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Objectives: To determine the impact of robotic surgery on patient’s access to minimally invasive surgery (MIS) for hysterectomies performed in California

Methods: Vaginal, laparoscopic, robotic and total abdominal hysterectomies performed in California between 2008 and 2011 were identified in the OSHPD database using ICD-9 codes. Vaginal, laparoscopic, and robotic hysterectomies comprised the MIS group and were compared to total abdominal hysterectomies. A multivariate analysis was performed to determine independent predictors of access to MIS.

Results: There were 174,325 hysterectomies performed between 2008 and 2011. Of all hysterectomies, 48% were performed by a MIS approach. The MIS growth rate was 13.8% between 2008 and 2011, comprising only 41.7% of total hysterectomies in 2008 and growing to 55.4% by 2011. The robotic hysterectomy growth rate showed the strongest correlation to the MIS growth rate (r=0.937, p<0.0057). Both the abdominal and vaginal hysterectomy rates declined over the 4-year period by 13.8% and 1%, respectively.

After adjusting for year, age, Charlson score, hospital volume, and insurance type, African Americans were 60% less likely to undergo hysterectomy by MIS than Caucasians (adjusted OR=0.40, 95% CI: 0.38 -0.41).

Discussion: Access to minimally invasive surgery for hysterectomies grew between 2008 and 2011. The growth rate is strongly correlated to the growth rate of robotic surgery. Despite an overall growth, disparities exist in access to MIS and are most significant for African American women when controlling for other variables.
LASER VAPORIZATION IN VULVAR INTRAEPITHELIAL NEOPLASIA (VIN), VAGINAL INTRAEPITHELIAL NEOPLASIA (VAIN) AND CONDYLOMATA ACUMINATA

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Introduction:
The objective: evaluate laser surgery technique in patients with: VIN 2/3, VAIN, or condylomata acuminata, putting emphasis on oncological criteria, feasibility, security and learning curve. Prospective and descriptive study. Show our initial experience, results and the follow up of 15 patients.

Material and Method:
15 patients: VAIN 2/3, VIN 2/3 or condylomata acuminata; diagnosed between July, 2011 - May, 2014. 6 (40%) laser surgery for condyloma acuminate were performed; 1 was an immunosuppressed patient with areas of VIN 2/3. 6 (40%) with VAIN 2/3 and 1 (7%) with VAIN 1. 2 (13%) with diagnosis of VIN II and 1 (7%) with VIN 1 and persistent pruritus. The results were expressed in medians.

Results:
Surgical time: 20 minutes. Biopsy was taken in 13 patients (87%). 14 (93%) the ablative therapy was outpatient. Complete response in 7 (47%). Persistent in 2 (13%). Recurrence before one year as of surgical date in 4 (27%); 2 were treated with topical 5-fluorouracil, 1 with radiation therapy, and 1 with Imiquimod. Recurrence after the second year as of surgical date in 2 (13%) cases: 1 required a revaporization, while the second was treated with tricloroacetic acid (TCA). None reported morbility or mortality.

Conclusions:
Laser vaporization is an excellent alternative in treatment of lesions in vulva or vagina. Feasibility, secure, outpatient. However it requires specific training and specialized equipment, with short learning curve. Complications are rare. Laser vaporization vs. excisional procedures: no significant differences in recurrence or persistent. Nevertheless advantages of ablation treatment are cosmetics results.
**IGCS-0107**  
Vulvar and Vaginal Cancer  

**PROGNOSTIC SIGNIFICANCE OF TUMOR SIZE IN SQUAMOUS CELL CARCINOMA OF THE VULVA**  
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**Objectives:**  
To evaluate the tumor size significance in a subgroup of patients with locoregional vulvar cancer which may be radically resected. Also, to determine whether a cut off value for tumor size may be defined.  

**Material & Methods:**  
Retrospective study. It included 105 patients (pts) between January/1995 - January/2012, with primary vulvar squamous cell carcinoma, stromal invasion > 1mm and a preoperatively tumor size > 2 cm. They underwent radical surgery as primary treatment (radical vulvectomy or local wide excision) and complete bilateral inguino-femoral lymphadenectomy. Patients were staged or re-staged according FIGO 2009. Stages IA and IV were excluded. Clinical & pathological tumor size were compared and analyzed, being stratified into lesions between > 2-3.99 cm, 4-5.99 cm, 6-7.99 cm and ≥ 8 cm. Age, histological grade, stage, lymph node status, OS and DFS, and follow-up were also considered.  

**Results:**  
Age: 67 years (range: 36-83). Follow-up: 21 months (range: 3-120). 2-year OS and DFS were 48% and 40% respectively. Eighty three patients (79%) had recurrent disease. Time to relapse: 12 months. A significant difference was seen in the OS analysis comparing tumors >2-3.99 cm to 4-5.99 cm (P =0.004) and 4-5.99 to 6-7.99 cm (P = 0.000). No significant difference was observed comparing tumors 6-7.99 to ≥ 8 cm (P = 0.647). After multivariate analysis, tumor size and stage were the only independent prognostic factors for DFS and OS. For tumor size, the risk for failure to survive was 2.8 times higher for patients with a tumor size between 4-5.99 cm (hazard rate [HR] = 2.85); 16 times for 6-7.99 cm (HR = 16.0) and 20.1 times for ≥ 8 cm (HR = 20.1), compared with tumor size >2-3.99 cm.  

**Conclusions:**  
A clear cut-off value in tumors ≥ 6 cm, from which value, survival drops remarkably. This could be important to tailor the treatment for patients with bulky primary tumors.