**TEMPORAL AND GENERATIONAL TRENDS OF HUMAN PAPILLOMA VIRUS (HPV) ASSOCIATED CANCERS REGISTERED BETWEEN 1985-2009 IN ENGLAND**

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**Introduction:** HPV is responsible for nearly all cervical and substantial number of oro-pharyngeal and ano-genital cancers. The increase in cervical cancer incidence in young women in England is thought to be due to a greater exposure to HPV.

**Methods:** We analysed all HPV-associated cancers in England between 1985-2009 with Joinpoint® regression and age-period-cohort modelling using intrinsic estimator. Socio-economical risk factors (economic activity, smoking, contraception, pregnancy terminations and sexually transmitted disease (STDs)) were analysed.

**Results:** Overall age standardised incidence of HPV-associated cancers except cervical cancer increased during 1985-2009 period.

![Graphs showing trends of HPV-associated cancers](image)
The incidence oro-pharyngeal, anal, penile and vulval cancer increased annually by an average of 2.7, 3.4, 1.4 and 0.4 per 100000 respectively. Incidence of cervical cancer reduced annually by an average of 2.2/100000, however the beneficial effect of screening reached plateau by 2004 and incidence increased between 2005-09. Cohort analyses revealed that the incidence of HPV-associated cancers has either levelled out or increased in cohorts born since 1940.

[Cohort analyses]

Substantial rise in HG-CIN is observed throughout the study period and in cohort born since 1940. Socio-economic factors remained stable or improved during the study period however incidence of STDs increased significantly in younger age-groups.

**Conclusion:** The incidence of HPV-associated cancers in England is rising. Cohorts born since 1940 are the most affected. Our results supports rising prevalence and greater exposure to HPV infection. These results have significant implications for the screening and vaccination programme.
UNDER-REFERRAL OF WOMEN WITH HEREDITARY ENDOMETRIAL CANCER TO GENETIC SERVICES: SUGGESTIONS TO FACILITATE REFERRAL OF SUSPECTED LYNCH SYNDROME PATIENTS

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Purpose: Current evidence suggests many individuals at risk of carrying an inherited mutation in a cancer-associated gene based on their personal/family history of cancer are not referred for genetic assessment. This study evaluated the rates and patterns of referral of women diagnosed with endometrial cancer to genetic services in Queensland, Australia.

Methods: For women diagnosed with endometrial cancer between May 2005 and December 2007, data were linked from three sources: a research study with detailed family history information; a major public hospital clinical database; the public genetic service provider referral database. We determined the percentage of women who could have been referred to genetic services based on hereditary cancer syndrome criteria, and the percentages who were referred and attended their scheduled appointments.

Results: Research data indicated that 236/397 (59%) of women with endometrial cancer treated at a major referral hospital had a personal/family history of cancer, including 45 (11%) who fulfilled Amsterdam II criteria indicative of Lynch hereditary cancer syndrome. However, any form of family history was noted in the hospital records of only 61 (15%) women, including 22 (49%) of those meeting Lynch criteria. Only 13 women (4 meeting Lynch criteria) were referred for genetic assessment, most often by their general practitioner (39%). Twelve women attended their appointments while the 13th died before she could do so.

Conclusions: Clinical records indicate poor recognition of family history and referral to genetic services for women with possible hereditary endometrial cancer. Application of research methods to document family history may facilitate automated referral for genetic assessment.
YOUNG DOCTORS’ SUMMIT

DNA POLYMERASE Ζ AS A PROGNOSTIC BIOMARKER FOR CERVICAL CARCINOMA

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Objective: DNA Polymerase ζ (Polζ), an error-prone DNA polymerase involved in translesion DNA synthesis, plays a significant role in the cytotoxicity, mutagenicity, and chemoresistance of several cancers. The association of Polζ with chemoradiation resistance and prognosis of cervical cancer patients needs exploration.

Methods: One hundred and twenty-three patients with squamous cell carcinoma of cervical cancer (CSCC) who had adjuvant concurrent chemoradiation therapy after radical surgery treated at Fudan University Shanghai Cancer Center between 2008 and 2009 were enrolled in this study. We tested their in vitro platinum resistance using the MTT method and the expression of Polζ in paraffin-embedded tissue samples using immunohistochemistry.

Results: Expression of Polζ was detected in 22% (25/116) of the specimens. The median in vitro inhibition rate of tumor cell growth by cisplatin, carboplatin, nedaplatin, and oxaliplatin was 80%, 37%, 78% and 51%, respectively. Among the tumor-related variables, FIGO stage (adjusted HR 6.7, 95% CI 1.7-26.4, P=0.007) and the Polζ protein expression (adjusted HR 6.5, 95% CI 1.7-25.0, P=0.006) were found to be significant predictors of progression-free survival (PFS) for the multivariate analysis. Kaplan-Meier survival estimates showed that the patients with high stage and Polζ-positive expression had a significantly shorter PFS. However, the association between Polζ expression and in vitro platinum-inhibition rates was not significant.

Conclusion: Polζ expression can be used as the predictor for poor prognosis, which might be caused by the potential chemoradiation resistance of the patients. The mechanism deserves further exploration.
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HUMAN PAPILLOMAVIRUS DETECTION IN MENSTRUAL BLOOD IN PATIENTS WITH HIGH RISK CERVICAL HPV POSITIVITY

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Background: Many females are reluctant to participate in cervical cancer screening program due to embarrassment and pain from pelvic examination. In several studies, the use of non-invasive HPV testing is found to be highly acceptable to women and increases participation rate. Menstrual blood (MB) HPV testing is completely non-invasive technique.

Objective: To evaluate the effectiveness of MB-HPV testing and its clinical outcome.

Methods: 40 patients (mean age 35.4 years, range 22-52 years) with positive result of cervical high risk (hr)HPV by Linear array HPV testing (Roche, USA) were recruited from December 13, 2011 to March 9, 2012. Menstrual blood collection must be performed within 28 days after cervical HPV testing as inclusion criteria. Sanitary napkins were provided at Chulabhorn Hospital. Then, menstrual blood specimens were sent to the laboratory and kept in refrigerator at 4 °C. Next, a small piece (1.5 x 1.5 x 0.2 cm) of interested part of napkins was collected and gone through DNA extraction using QIAamp DNA Mini kit. After that, HPV genotyping was analyzed by Linear Array (two round of PCR step).

Results: Four women were excluded. Of 36 cervical hrHPV positive women, 20 were menstrual blood hrHPV positive. The hrHPV and type specific concordance rates were 55.56% and 52.78% (19/36), respectively.

Conclusion: MB-HPV testing is moderately representative to determine cervical HPV status. These preliminary results suggested that MB-HPV testing could be a potential non-invasive marker for cervical HPV infection. Further development of this technique to increase concordance rate is suggested.
YOUNG DOCTORS’ SUMMIT

TUMOR-ASSOCIATED LYMPHOCYTES ATTENUATE TUMOR IMMUNITY TO PROMOTE PROGRESSION OF SEROUS ENDOMETRIAL CANCER VIA STAT1 PATHWAY

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Objectives: Serous papillary endometrial cancers (SPEC) are highly progressive with poor prognosis. Tumor infiltration of immune cells (TII) is frequently observed in SPEC. TII was initially regarded as an attempt by the host organism to combat malignancy, but it has been revealed to promote tumor growth, facilitate tumor cell survival, and aid in tumor migration. As the precise mechanism of TII in SPEC still remains unclear, genetic analysis for SPEC was performed in the aspect of tumor immunity.

Methods: An expression microarray of endometrial cancers, GSE2109, was bioinformatically analyzed to detect a SPEC-specific pathway with putative downstream TII-correlating genes, which expression in endometrial cancer was further determined by immunohistochemical staining with clinical samples. Using a SPEC cell line, SPAC-1L, cellular proliferation, migration, and invasion in vitro; and tumorigenesis in vivo, were assessed with or without manipulation of the pathway genes.

Results: Microarray analysis revealed STAT1 pathway was highly activated in SPECs, confirmed by immunohistochemical staining on human SPEC tissue. STAT1 downstream genes, intercellular adhesion molecule-1 (ICAM-1) and programmed cell death 1 ligand-1 (PD-L1), co-localized with tumor-associated lymphocytes at the frontier site of invading tumor cells. The expression of ICAM-1 and PD-L1 were induced in SPAC-1L cells by IFN-γ, and this induction was significantly associated to the capability of cellular proliferation, migration and invasion. STAT1 suppression also attenuates in vivo tumorigenesis significantly.

Conclusions: These results indicate that STAT1 and its downstream genes, ICAM-1 and PD-L1, may play a certain role in association with the tumor-associated lymphocytes in endometrial cancer progression.
YOUNG DOCTORS’ SUMMIT

RISK ASSESSMENT MODEL FOR OVERALL SURVIVAL IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER TREATED WITH DEFINITIVE CONCURRENT CHEMORADIOThERAPY

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Aims: The aim of this study was to develop a risk assessment model for predicting the probability of 3-year survival after definitive concurrent chemoradiotherapy (CCRT) in locally advanced cervical cancer.

Methods: Between 1998 and 2008, 209 patients of cervical cancer were treated with definitive CCRT in our institution. Before CCRT, Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG-PET/CT) was performed in 91 patients. Multivariate analysis using Cox proportional hazards regression model was performed. The authors developed a nomogram based on this Cox model. Internal validation of the nomogram was performed with bootstrapping and performance was assessed by concordance index and a calibration curve.

Results: The median age was 55 years (range, 26-78). International Federation of Gynecology and Obstetrics (FIGO) stage included: IB2 (9), IIA (16), IIB (129), IIIA (3), IIIB (42), and IVA (10). Histology included: squamous (193), adenocarcinoma (9), adenosquamous (4), and small cell (2). Median follow-up period was 51 months (range, 6-151) and 50 (23.9%) deaths of disease had occurred. By multivariate regression analysis, histology, tumor size, and paraaortic lymph node metastasis were identified as independent predictors for overall survival. Whether 18F-FDG-PET/CT was performed before CCRT was not a significant factor affecting for overall survival. The nomogram for predicting the 3-year survival was constructed incorporating these 3 variables. The concordance index was 0.69. The predictive ability of the nomogram proved to be superior to FIGO stage (P< 0.05).

Conclusion: The constructed nomogram appears to be a better predictive model for overall survival than the FIGO staging system.
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MULTI-CENTER GENE EXPRESSION ANALYSIS OF MULLERIAN LOW-GRADE AND HIGH-GRADE SEROUS CARCINOMA HIGHLIGHTS GENES POTENTIALLY INVOLVED IN CHEMOTHERAPY RESISTANCE

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Objectives: Gene expression profiles of mullerian low-grade serous carcinoma (LGSC) and high-grade serous carcinoma (HGSC) were examined to identify differentially expressed genes involved in carcinogenesis and chemotherapy response.

Methods: 27 LGSC and 44 HGSC from publicly available datasets were analyzed. All specimens were laser-capture microdissected and analyzed on Affymetrix U133plus2 gene-chip microarray platform. Differentially expressed genes were filtered and subjected to a t-test with a Benjamini and Hochberg multiple testing.

Results: Unsupervised hierarchical cluster analysis showed segregation of LGSC from HGSC. HGSC tumors previously classified as primary ovarian carcinoma or primary fallopian tube carcinoma clustered together irrespective of their designated origin. 475 probe-sets were at least 2 fold different between the LGSC and HGSC. LGSC were found to overexpress KLF4 and its target p21/WAF1 relative to HGSC. These proteins have both tumor suppressive and oncogenic effects.

Conclusions: Our findings support the hypothesis that serous mullerian carcinoma may develop through two different pathways yielding two distinct malignancies- LGSC and HGSC. Gene expression analyses demonstrated overexpression of KLF4 and p21/WAF1 in LGSC. The key role of these proteins in proliferation inhibition may contribute to the differential response of LGSC to standard chemotherapy. Similarly, a novel LGSC-associated gene, Clusterin, encodes for a secreted protein previously shown to prevent paclitaxel-induced apoptosis of ovarian cancer cell lines. Suppressing the levels of these proteins may increase clinical response to chemotherapy in patients with LGSC. In addition, the genetic profiles identified in this study may potentially be used in developing disease-specific, targeted therapy for LGSC and HGSC.
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SENTINEL LYMPH NODE DETECTION AND ACCURACY FOLLOWING INTRA-OPERATIVE CERVICAL INJECTION IN ENDOMETRIAL CANCER

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Objective: To evaluate the detection rate and diagnostic accuracy of sentinel lymph node (SLN) mapping using intra-operative cervical injection of patent blue and filtered 99mTc-sulfur colloid (99mTc-SC) in endometrial cancer patients.

Methods: Prospective evaluation of the first 100 endometrial cancer patients undergoing SLN mapping using patent blue (0.8 ml) and filtered 99mTc-SC (250 µCi in 0.2 ml) combined in 1 ml syringes (4 total) in the O.R.. 2 syringes were injected at the 3 o’clock and 2 at the 9 o’clock position in the cervix, one stromal and one submucosal. Patients underwent robotic-assisted lymphatic mapping with frozen section, hysterectomy, BSO, and complete lymphadenectomy, including peri-aortic nodes in grade 2 and 3 tumors.

Results: Since December 2010, endometrial cancer patients underwent SLN mapping. No complications or anaphylactic reactions were noted. 92% of patients had at least one SLN detected, 66 of 92 had bilateral SLNs detected, and in 15 cases the SLN was in the peri-aortic area. 11% of patients had lymph node metastases. The SLN was the only positive node in 36% of the cases with positive nodes. Sensitivity was 89% with 1 false negative result, yielding a negative predictive value of 99% (95% CI 93-100), and negative likelihood ratio of 0.11 (95% CI 0.02 - 0.70).

Conclusion: SLN biopsy using intra-operative cervical injection of patent blue and filtered 99mTc-SC in endometrial cancer patients is feasible, safe, and yields encouraging detection rates. Further investigations are planned by the Society of Gynecologic Oncology of Canada SLN Communities of Practice group.
YOUNG DOCTORS’ SUMMIT

PREVALENCE OF LYMPHOCYSTS AFTER PELVIC AND PARAAORTIC LYMPHADENECTOMY AND MINIINVASIVE TREATMENT WITH US GUIDED DRAINAGE

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Background: Pelvic lymphadenectomy is associated with significant complications including lymphocyst formation and related morbidities. Prevalence of lymphocysts after oncogynecological procedures is being reported in a wide range 2-32%.

Objective: To assess the prevalence of asymptomatic and symptomatic lymphocysts in our group and evaluate ultrasound guided drainage in treatment of symptomatic lymphocysts.

Results: In the years 2006-2010, we performed 472 pelvic and 225 paraaortic lymphadenectomies. All patients were followed by pelvic and abdominal ultrasound at 3 month intervals. Together 137 pelvic (29%) and 1 paraaortic (0.44%) lymphocysts have been detected, however, only 27 (3.87%) of them were symptomatic (signs of inflammation in 15 cases; pain, lymphoedema, dysuria or ureter obstruction in 12 cases) and required intervention. In these 27 patients, the ultrasound guided drainage was used with Fr 15 pig-tail catheter left for 2-3 days under antibiotics. All the patients with non-inflammatory lymphocyst and 7 with inflammation were successfully treated (70.4%). In 8 pts. from inflammatory group, subsequent surgery was needed. There were no severe complications related to the drainage in the whole group.

Conclusions: Formation of lymphocyst was common finding after pelvic lymphadenectomy and rare after paraaortic lymphadenectomy. However, only in minority of patients the lymphocyst becomes symptomatic and requires intervention. Ultrasound guided drainage with insertion of catheter for 2-3 days was safe and efficient method for miniinvasive treatment of symptomatic non-inflammatory lymphocysts, but failed in about half of inflammatory cases.

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YOUNG DOCTORS' SUMMIT

A PHARMACOGENETIC ASSESSMENT OF SINGLE NUCLEOTIDE POLYMORPHISMS WITH SEVERE TOXICITY OF (NEO-)ADJUVANT PACLITAXEL AND CARBOPLATIN IN OVARIAN CANCER

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Introduction: We assessed the impact of single nucleotide polymorphisms (SNPs) on the occurrence of severe toxicity events in ovarian cancer patients receiving (neo-)adjuvant chemotherapy with paclitaxel and carboplatin.

Materials and methods: A panel of 26 SNPs in 17 genes involved in the pharmacodynamics of taxanes and DNA detoxification or repair of platinum was selected based on an extensive literature survey. SNPs were genotyped in the germline DNA of 322 patients using Sequenom MassARRAY and correlated with the occurrence of neurotoxicity (grade 2-4), anemia (3-4), neutropenia (4), trombopenia (3-4) and febrile neutropenia by logistic regression while correcting for age and Body Mass Index (BMI). Cases were retrospectively evaluated through electronic chart review.

Results: The risk of grade 3-4 anemia was increased in patients carrying a variant allele for rs1128503 (ABCB1) (p=0.037, OR=1.578, 95%CI =1.028-2.424), rs11615 (ERCC1) (p=0.030, OR=1.555, 95%CI =1.043-2.318), rs12762549 (ABCC2) (p=0.006, OR=0.557, 95%CI =0.366-0.846) and rs363717 (ABCA1) (p=0.001, OR=1.980, 95% CI=1.302-3.011). The risk of febrile neutropenia was increased in patients carrying a variant allele of rs1042522 (TP53) (p=0.026, OR=2.019, 95% CI=1.088-3.747). An increased risk of trombopenia was associated with variation in rs1045642 (ABCB1) (p=0.045, OR=1.564, 95%CI=1.010-2.423) and rs4986910 (CYP3A4) (p=0.032, OR=4.485, 95% CI=1.139-17.659). Neurotoxicity was not significantly correlated with any of these SNPs.

Conclusion: Genetic variability in the ABCB1, ABCC2, ABCA1, ERCC1, TP53, CYP3A4 genes was significantly associated with severe hematologic toxicity but not with neurotoxicity in ovarian cancer patients treated with first-line paclitaxel-carboplatin.
MICRORNAS ASSOCIATED WITH LYMPHNODE METASTASIS IN CLINICAL STAGE I ENDOMETRIOID ADENOCARCINOMAS OF THE UTERINE CORPUS: A GYNECOLOGIC ONCOLOGY GROUP STUDY

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Objective: Lymphadenectomy is routinely included in the surgical staging of endometrial cancer, however, most patients with clinical stage I endometrioid endometrial cancer will have negative lymph nodes. Clinico-pathological parameters can predict lymphnode metastasis with modest success. Our purpose was to evaluate miRNA expression profiles in clinical stage I endometrioid endometrial cancers. We further sought to develop a miRNA classifier that could predict lymph node metastasis in clinical stage I endometrioid endometrial cancers.

Methods: Fifty surgical stage I tumors and 50 surgical stage IIIC tumors were obtained from the Gynecologic Oncology Group tumor bank from patients with clinical stage I endometrial cancers. Messenger RNA was extracted from the frozen tumor samples and microarray analysis performed. Differentially expressed miRNAs were identified and from these miRNAs, a classifier was developed using multiple Support Vector Machine-Recursive Feature Elimination algorithm.

Results: We identified 169 miRNAs that were differentially expressed between surgical stage I and stage IIIC tumors. From these miRNAs, a 16 miRNA classifier was developed which correctly identified stage I or stage IIIC with an accuracy of 97%. The sensitivity and specificity of the classifier was 96% and 98% respectively.

Conclusions: We have identified miRNAs associated lymph node metastasis in clinical stage I endometrioid endometrial cancers. Further, we have identified a miRNA classifier that can accurately determine the presence of lymph node metastasis in patients with clinical stage I endometrioid endometrial cancer. Further studies are needed to validate our results.
YOUNG DOCTORS’ SUMMIT

OUTCOME AND QUALITY OF LIFE AFTER PELVIC EXENTERATION FOR RECURRENT ENDOMETRIAL AND CERVICAL CANCERS

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Background: Pelvic exenteration has been used as a curative operation in recurrent malignancies. However, treatment-related morbidity is over 50% in radiated pelvises.

Objectives: To evaluate the outcome, morbidity and quality of life after pelvic exenteration.

Methods: Patients who underwent an exenteration for recurrent cervical or endometrial cancer in Institut Curie from 1999 to 2011 were studied. The EORTC QLQ-C30 and QLQ-CX24 questionnaires were sent to patients alive in January 2012.

Results: We identified 25 patients: 17 (68%) had cervical cancer and 8 (32%) endometrial cancer. 92% of patients received radiotherapy. All patients had a central pelvic recurrence, in a median time of 30 months [4-384]. Exenteration achieved complete tumoral resection in 22 patients (88%). Early complications needing a re-laparotomy occurred in 9 patients (36%) (insufficiencies of intestinal or ureteral anastomosis and pelvic abscesses). Late complications included 2 (8%) fistulas, 2 (8%) intestinal occlusion and 1 (4%) ureteral stenosis. Progression Free (PFS) and Overall survival (OS) rates were better in cervical than in endometrial cancer (median DFS in months 17 [2-145] vs 9.5 [3-21], p= 0.064, median OS in months 20 [2-145] vs 13 [4-42], p=0.019). 70% of contacted patients answered the questionnaires. Mean global quality of life score was 45 on a scale of 100, none of the patients had a sexual activity.

Conclusions: Morbidity of pelvic exenteration remains high and quality of life is impaired. Endometrial cancer is associated with a poorer prognosis. In those patients, the benefit of exenteration should be discussed compared to supportive care for palliative treatment.
Educational Symposium: INTERNATIONAL HEALTH

PREVALENCE OF HIGH RISK HUMAN PAPILLOMA VIRUS GENOTYPES IN CERVICAL CARCINOMA, LOW-GRADE, AND HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS IN JORDANIAN WOMEN

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Objective: The aim of this study is to assess high risk human papillomavirus (HR-HPV) prevalence and genotypes’ distribution in invasive cervical cancer and its precursors in Jordanian patients to provide baseline information for screening and prevention.

Methods: A total of 124 different specimens of formalin-fixed, paraffin embedded samples, including 18 low-grade squamous intraepithelial lesions (LSIL), 28 high grade squamous intraepithelial lesions (HSIL), and 78 cervical cancers (CC) were included in this study. HPV detection and typing was done using HPV High Risk Typing Real-TM Kit (Sacace Biotechnologies, Italy) that enables the concomitant detection of the 12 most common HR-HPVs.

Results: Overall, HR-HPV prevalence was 87.2%, 78.6%, and 72.2% in CC, HSIL, and LSIL respectively. Genotype 16 was the most predominant in all cervical lesions, detected in 53.8%, 46.4%, and 38.9% of CC, HSIL, and LSIL. Among all HPV genotypes, HPV-16 and HPV-18 are found separately or together in 50% of LSILs, 60.7% of HSILs and 76.9% of cervical cancer specimens. HPV 31 was the second most common type detected in LSILS (22.2%) and HSILS ((21.4%). HPV 45 was the third most common type detected in cervical cancer (11.5%).

Conclusions: The prevalence and genotypes distribution patterns of HR-HPV types among patients with cervical cancer and its precursors in Jordan are similar to known international patterns. The results of this study provide baseline information on the HPV type distribution, which may guide the development of cervical cancer prevention and control programs in Jordan.
Educational Symposium: INTERNATIONAL HEALTH

CERVICAL CANCER TRANSITION IN LESOTHO, A REVIEW AFTER TEN YEARS AT QUEEN ELIZABETH II HOSPITAL

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Background and aim: Cervical cancer is the most common cancer among women in Lesotho, with Incidence rate of 66.7(ASR) in 2006. HIV prevalence in Lesotho has increased from 0.8% in 1990 to 23.5% in 2009. Aim is to study the effect of HIV on cervical cancer trend in Lesotho.

Methods: Comparative study of cervical cancer records of cases that were managed between 1997-2000 and 2007-2010. Demographic and histological characteristics were studied for any difference which may have been due to the HIV epidemic. Data entry and Statistical analysis were done with Epi info.

Results: 240 cases of cervical cancer (1997-2000) were compared with 349 (2007-2010), the mean age at diagnosis were 53.52 (95% CI 51.78-55.26) and 52.27(50.79-53.75) with a mean decrease of 1.25 years. The distribution curve for the 1997-2000 had a single peak age group 51-55 while the 2007-2010 arms had a bimodal peak at age group 46-50 and 61-65. The proportion of women age 40 years and below rose from 18.4% to 24.5 % (chi square =2.96, P value 0.085). All patient age 35 and bellow in both arms were HIV positive. The proportion of Adenocarcinoma increased from 4.3% to 7.2% while that of squamous cell carcinoma decrease from 94.6% to 86.9%. The proportion of other histological types increase from 1% to 5.8%.

Conclusions: There is a decrease in mean age for cervical cancer in Lesotho, increase in the proportion of women presenting at early age, Adenocarcinoma and other variants, HIV is associated with early cervical cancer.
Educational Symposium: INTERNATIONAL HEALTH

ADJUVANT CHEMOTHERAPY FOR LOCALLY ADVANCED CERVICAL CANCER

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Aim: To evaluate the role of adjuvant chemotherapy (ACT) after concurrent chemoradiation therapy (CCRT) for locally advanced cervical cancer (LACC).

Methods: We searched MEDLINE database to identify studies which assessed the efficacy of ACT after CCRT in LACC. Characteristic features of the patients, treatment and outcomes after treatment were reviewed.

Results: We identified four prospective single arm studies, one match case comparison study, and four randomized controlled trials (RCTs) on this subject. These studies had various characteristic features of the patients, with different chemotherapy regimens and patterns of administration. All studies and RCTs showed that ACT yielded a higher response rate than simply RT or CCRT. However, its survival benefit was inconsistent. Only three RCTs could demonstrate survival advantage of adjuvant chemotherapy. Some imbalances between the study and control arms in these positive trials were observed: one trial applied radiation alone in the control arm vs CCRT followed by ACT in the study arm; one trial used only single agent during CCRT in the control arm vs doublet chemotherapy during CCRT prior to ACT in the study arm; and the last trial provided CCRT alone in the control arm vs neoadjuvant chemotherapy prior to CCRT followed by ACT in the study arm. For the one negative trial, oral chemotherapy was used as ACT when unpredictable drug absorption might have led to a negative result.

Conclusions: A definite conclusion cannot be made regarding the survival benefit of adjuvant chemotherapy after concurrent chemoradiation therapy for locally advanced cervical cancer.
Educational Symposium: INTERNATIONAL HEALTH

CHALLENGES OF PALLIATIVE CANCER CARE AT FEDERAL MEDICAL CENTRE, AZARE (FMCA)

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Federal Medical Centre, Azare, Nigeria

Objective: To identify challenges of palliative cancer care at FMCA.

Materials: Tools of data collection were hospital records, world health report, interview with 115 randomly selected cancer patients at FMCA.

Methods: It is a hospital based study.

Results: High cancer mortality in developing counties demonstrates that cancer control is poor and less effective.

The FMC Azare is a tertiary health centre in a rural area, providing care to people in a radius of greater 200Km. The major challenges to cancer care, especially palliative care, identified were late presentation by patients, lack of trained cancer care health professionals and lack of resources for managing advanced disease.

The delay in presentation is to a variety of factors but commonly due to lack of knowledge and awareness of signs and symptoms of cancer; poverty, in rural Nigeria, cost of health care is often "catastrophic" defined as exceeding 10% of annual household income so many can't afford hospital treatment resorting to traditional treatment preventing early diagnosis; some cultural beliefs that ailments are part of witchcraft that requires spiritual cleansing first. Poor health services and inadequate skilled manpower leads to delay in diagnosis, inadequate investigations and inappropriate therapy. Surgeons skilled in cancer surgery are unavailable; Radiotherapy is mostly unaffordable. Chemotherapy is not freely accessible and costly. There is lack of pain relief, Morphine is simply not available.

Most patients receive available treatment rather than optimal treatment and sadly sent home to die painful and distressing death.

Conclusion: Cancer is a growing health burden in Africa especially Nigeria so cancer control must be integral aspect of health policy. There should be massive investment in manpower and infrastructure development in cancer control by government and attempts to recover health care costs from patients causes poor health seeking behavior so policy of user fees should be withdrawn in rural areas.
Educational Symposium: INTERNATIONAL HEALTH

DIFFERENCE BETWEEN HIV INFECTED AND HIV NON-INFECTED WOMEN WITH CERVICAL PRE-NEOPLASIA: HPV SEROTYPES ASSOCIATED WITH CERVICAL INTRA-EPITHELIAL NEOPLASIA

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Objectives: Human papillomavirus (HPV) type distribution differs between population groups, countries and regions. Viral types associated with pre-neoplastic lesions may also be different between HIV positive and immunocompetent women.

Methods: We report incidental and carcinogenic HPV types found with DNA analysis in a cohort of 151 women presenting for treatment of cervical pre-neoplasia, in a setting with a high prevalence of HIV infection. Hundred and three tested HIV positive, 40 HIV negative and 8 unknown or declined testing. Of the 143 patients with HIV results, 128 presented with HSIL on Pap smear. In the HIV positive group, 83.6% had CIN II/III compared to 67.5% of HIV negative patients. HIV negative women had an average of three HPV type(s), HIV positive women had five types (p=0.0001). HPV 16 and/or 18 was present in 51.5% of HIV positive and 42.5% of HIV negative women. Immunocompetent women had below two high-risk HPV types (zero to three), while immunodeficient women had just below three high-risk HPV types (zero to five) (p=0.0063). From our data it appears that the prevalence of HPV 33, 35 and 51 are most linked to immunosuppression.

Conclusion: HIV infection contributes a large burden of cervical disease in South Africa. We confirm previously reported high numbers high and low-risk HPV types in HIV infected women. Without viral type cross-protection, current HPV vaccines would be extrapolated to prevent almost 49% of high-grade lesions in our population and suggest that these vaccines may even be more effective in women infected with HIV.
Educational Symposium: INTERNATIONAL HEALTH

OUTCOMES FROM A RADICAL HYSTERECTOMY TRAINING PROGRAM IN A LOW RESOURCE SETTING

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Objective: To evaluate the safety of Radical Hysterectomy surgery in a low resource setting.

Study methods: Data from 40 radical hysterectomies performed were reviewed. Intra-operative and postoperative complications, postoperative voiding were used as surrogate measures to assess the safety of the surgery. The results were compared with published data on complication rates in both a low and high resource setting using chi-square analyses.

Results: At presentation, 25 of the cases had operable lesions (FIGO Stage ≤IIA); 15 more received neoadjuvant chemotherapy for downstaging prior to surgery. Of 40 cases done, 3 (9.1%) resulted in one or more complications. One patient had a major intraoperative hemorrhage requiring blood transfusion and ligation of the external iliac vein. Postoperative complications included fascial dehiscence, deep vein thromboemolism, wound infection and fistula. 37 (92.5%) patients voided on their own by postoperative day 5 and all others by postoperative day 10. The complication rates were not statistically different (p > 0.05) to those documented in either a high or low-resource settings.

Conclusions: Radical hysterectomy in this setting is a high risk but high reward procedure. If complication rates are high, continuing with the program may not be justified. These analysis shows the surgery can be completed safely in this setting. With screening, more early stage cancers are identified and more women benefit from curative surgery.
Educational Symposium: INTERNATIONAL HEALTH

SURGICAL CAPACITY BUILDING IN GYNAECOLOGIC ONCOLOGY IN UGANDA

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Developing countries like Uganda bear a disproportionate burden of morbidity and mortality from cervical cancer. The vast majority of cancers are diagnosed at a late stage. Some screening for cervical cancer is now being offered. This enables detection of precancerous disease and early cervical cancers. Early cervical cancers, amenable to surgical treatment, will free up much needed radiation resources.

Currently, there are no Gynaecologic Oncologists in Uganda. Since 2008 there has been a Gynaecologic Oncology Division within the OB-GYN Department at Mulago National Referral Hospital affiliated with Makerere University College of Health Sciences. Gynaecologists at Mulago and Gynaecologic Oncologists from the University of British Columbia in Vancouver, Canada began collaborating in 2011 to work on building surgical capacity for gynaecologic cancer surgery. All stakeholders involved in cervical cancer care have been consulted and involved in the process. This includes the Uganda Ministry of Health, gynaecologists, pathologists, radiation oncologists, medical oncologists, nurses (ward and cervical cancer screening clinics), colposcopists, and leadership at the Uganda Cancer Institute, Makerere and Mulago.

Although surgical education was the thrust of the initial collaboration, the involvement of all partners has resulted in various opportunities to build capacity both at Mulago and the Uganda Cancer Institute. Working within the existing infrastructure is critical to the sustainability of any developments that come out of the collaboration. The next step is application of a surgical training module, developed by the Gynaecologic Oncologists of Canada(GOC), which includes teaching surgical techniques and mentoring in the operating room.
Educational Symposium: INTERNATIONAL HEALTH

HPV VACCINATION IN LOW-RESOURCE COUNTRIES: CURRENT EVIDENCE AND GLOBAL UPDATE

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Human papillomavirus (HPV) vaccination has the potential to reduce cancer deaths by more than 60% in developing countries, where more than 85% of the mortality occurs. Successful planning for HPV vaccine introduction in developing-country settings requires a comprehensive approach that addresses individual, interpersonal, community, structural, and policy factors that positively enable HPV vaccine uptake. Results from several country pilot programs, including PATH demonstration projects in India, Peru, Uganda, and Vietnam, have provided insight and evidence on acceptable and feasible delivery strategies that have resulted in high coverage of HPV vaccine among girls aged 10 to 14 years old. At least eight other low-resource settings have conducted small pilots with similar results, suggesting common factors for success and common barriers to implementation. The collective experience to-date suggests components of a strong foundation for successful HPV vaccine implementation that can be modeled by countries planning to introduce this vaccine into their national immunization programs. The financial support for vaccine procurement announced by the GAVI Alliance will provide developing countries with access to subsidized pricing for vaccine procurement, mitigating one potential barrier to rapid scale-up in those areas where the burden of cervical cancer is greatest. This presentation will summarize the global experience with HPV vaccine introduction in low-resource settings and its broader implications for the scale and pace of country adoption.
Educational Symposium: PATHOLOGY

CONTROVERSIAL ISSUES RELATING TO EPITHELIAL AND MESENCHYMAL NEOPLASMS OF THE UTERINE CORPUS

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The International Society of Gynecologic Pathologists (ISGP) formed a committee in July, 2011, to re-examine controversies involving the classification and nomenclature of gynecologic neoplasms, one subcommittee of which focused on epithelial and mesenchymal neoplasms of the uterine corpus. Controversial topics were solicited from the 15 committee members, and resulted in identification of about 40 issues. Definitive assertions about each of these issues were created and then initially voted upon by all committee members, the results of which displayed a high level of disagreement for most topics. Following this vote, each issue was assigned to 2 committee members who wrote a position paper supported by available literature. After circulation of the position papers, the subcommittee met and discussed the issues again, attempting to identify a consensus position. A consensus was then achieved for more than 25 of the issues. Examples of issues reaching consensus included the use of either EIN or modified WHO categories for classification of precursors to endometrioid adenocarcinoma, and that the distinction of endocervical gland involvement from endocervical stromal invasion is generally not reproducible, while there was felt to be insufficient data to determine the biologic significance of isolated tumor cells in pelvic lymph nodes, and there was no consensus as to whether endometrial polyps should be classified as an epithelial or a stromal neoplasm. The entire range of issues and the consensus positions will be presented, and their pragmatic significance will be discussed by Dr. David Mutch.
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Educational Symposium: PATHOLOGY

THE STROMAL ORIGIN OF SOME EPITHELIAL OVARIAN NEOPLASMS

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The most popular theory today for the origin of ovarian epithelial tumors is that they originate from the fallopian tube. I believe that some ovarian epithelial stromal neoplasms can develop from unremarkable mesenchyma, from areas that do not include epithelium, and since these lesions are almost out of nothing this could be called “fere ex-nihilo.” This proposal is based on embryologic evidence, animal studies, and clinicopathologic observations. Embryologic evidence: There is an intimate relationship between the undifferentiated mesenchyma and the origin of the mullerian duct. The mullerian duct appears to emerge from unremarkable mesenchyma. This concept should not be difficult to accept because the epithelial cells that line the celomic cavity originate from the mesenchyma underlying these epithelial cells; this is the reason for its designation, mesothelium. Evidence from experimental animal studies: In our previous studies with guinea pigs we have seen the development of de novo areas of endosalpingiosis in the ovarian stroma, the tumors started in the stroma as groups of epithelial cells, most likely derived from stem cells, and they arose simultaneously from multiple sites within the stroma. I would consider this a typical example of fere ex nihilo Evidence from clinicopathologic cases: there are several lesions that would be difficult to explain by origin from the fallopian tube or from metaplasia of the epithelium. These are lesions with stromal and epithelial components including endometriosis and adenofibromas. I believe there is enough embryologic, experimental, and clinical pathologic evidence that epithelial cells can develop from unremarkable mesenchyma (stromal- epithelial interaction), due to the effects of hormones, and this could be a different explanation for the development of ovarian neoplasms.
Educational Symposium: PATHOLOGY

UPDATE ON PATHOLOGY TERMINOLOGY - LOWER GENITAL TRACT

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The recognition that a significant proportion of lower female genital tract lesions are caused by HPV infection has led to the proposal that they should be classified primarily on the basis of whether they are related to HPV infection or not. The lower anogenital squamous terminology (LAST) project has recommended that HPV-associated squamous lesions of the lower anogenital tract are classified as low-grade and high-grade squamous intraepithelial lesions (LSIL and HSIL), which may be further classified by the applicable intraepithelial neoplasia subcategorization. In the vulva, this is consistent with the concept of differentiated (non-HPV-related) and undifferentiated/usual (HPV-related) vulvar intraepithelial neoplasia (VIN). In the vagina and cervix, almost all squamous lesions are HPV related, as are cervical adenocarcinoma in situ and usual type adenocarcinoma. Less common types of cervical adenocarcinoma, for example mesonephric, clear cell, gastric and minimal deviation adenocarcinomas, are not, however, associated with HPV infection. This primary subdivision of lesions based on their association with HPV may be therapeutically relevant, particularly for intraepithelial disease.
Educational Symposium: PATHOLOGY

ORIGINS OF OVARIAN CANCER - NON-SEROUS EPITHELIAL TUMORS

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Non-serous epithelial tumors of the ovary include endometrioid, clear cell, mucinous and transitional types. A combination of the increasing recognition of ovarian metastases; the more extensive sampling of ovarian tumors; and the generation of comprehensive molecular data has led to refinement of the classification of these tumors. When metastases are rigorously excluded, primary mucinous ovarian tumors are uncommon, are typically large and unilateral, and are associated with KRAS mutation. Primary ovarian low-grade endometrioid carcinomas show a close association with ovarian endometriosis and the molecular abnormalities identified in these tumors, for example ARID1A mutation, overlap significantly with those present in low-grade endometrioid carcinomas of the endometrium, implying similarities in pathogenesis. High-grade endometrioid carcinomas are more similar to high-grade serous than to low-grade endometrioid carcinomas. Clear cell carcinomas may arise in association with endometriosis but may also be seen in association with clear cell adenofibroma. High-grade 'transitional' carcinomas that are unassociated with Brenner tumors show significant similarities with high-grade serous carcinomas and many are likely to be variants of high-grade serous carcinoma. Malignant Brenner tumors, when strictly defined, are rare.
Educational Symposium: ROBOTICS

SURGICAL OUTCOME FOR ROBOTIC SURGERY IN THE MORBIDLY OBESE PATIENT WITH ENDOMETRIAL CANCER COMPARED TO LAPAROTOMY

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Introduction: Prior to the introduction of robotic surgery at our institution the majority of obese women of class II or greater (BMI >35) underwent a laparotomy for the management of endometrial cancer. Since November 2008 we have performed the majority of these cases in a robotic fashion. This manuscript presents the outcome of these women in comparison to a historical cohort of women treated with laparotomy.

Methods: Women with clinical stage 1 or 2 endometrial cancer and a Body Mass Index (BMI) greater than 35 Kg/m² treated with robotic surgery at our institution between November 2008 and November 2010 were compared to a historical cohort of similar patients who underwent laparotomy. Patient characteristics, operating room time, type of surgery, length of hospital stay and incidence of peri-operative complications were compared between the two groups.

Results: A total of 87 women were analyzed in this study (46 robotic, 41 laparotomy). The overall intra-operative complication rate is 6.9%. There is no statistical difference in age, number of co-morbidities, BMI, prior abdominal surgery, and operative complications between the women who underwent robotic surgery versus laparotomy. Post operative complication rates are higher in the laparotomy group (44% vs. 17.4% p=0.007) and hospital length of stay is also higher in the laparotomy group (4 vs. 2 days, p< 0.001). There is no difference in rates of (pelvic) lymph node dissection; however para-aortic node dissection is more common in the robotic surgery group.

Conclusion: Robotic surgery for the surgical management of the morbidly obese patient is shown to be safe and have less peri-operative complications compared to open surgery. Hospital length of stay is also significantly shorter with robotic surgery.
Educational Symposium: ROBOTICS

NEW CLINICAL DEVELOPMENTS, ROBOTICS & OVARIAN CANCER

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Despite the well established advantages of minimal invasive surgery (MIS) in the surgical treatment of endometrial and cervix cancer, staging and treatment of epithelial ovarian carcinoma remains a question of debate.

Since 1990, several studies about the use of laparoscopy in ovarian cancer were published. Prospective data and retrospective analyses have demonstrated the feasibility and the safety of laparoscopic approach in treatment of presumed early stage ovarian cancer and in re-operative surgery for incompletely staged EOC.

However, the use of minimally invasive surgery for advanced ovarian cancer is still controversial and data to support this approach are scant.

Robotic surgery, with its improved ergonomics and three dimensional immersion high definition visualization might extend the indications of MIS in advanced ovarian cancer, but the absence of haptics and the difficulty to access multiple abdominal quadrants represents a significant limitation.

This presentation analyzes our recent data on robotic surgery in advanced stage ovarian cancer performed mainly at the time of interval cytoreduction following neoadjuvant chemotherapy and reviews the information available on minimally invasive surgery and ovarian cancer.
Educational Symposium: WHAT IS INDIVIDUALIZED MEDICINE?

OPPORTUNITIES FOR INDIVIDUALIZED THERAPIES FOR CERVICAL CANCER

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While the incidence of cervical cancer has declined significantly in the Western world, ethnic disparities remain in terms of increased mortality and morbidity. Furthermore, this disease continues to be a significant burden on developing countries, with cervical cancer currently ranked as the second most common cause of cancer-related morbidity and the third most common cause of mortality worldwide. Treatment of cervical cancer has typically been viewed as surgical with possible adjuvant therapy versus initial radiotherapy and platinum-based chemotherapy when limited to the pelvis. Prognosis and therapy for patients with advanced or recurrent disease is dependent upon the site of recurrence and ability to pursue curative therapy. This presentation will briefly review the management of cervical cancer, including studies that have evaluated the treatment of distant metastasis or recurrent disease, focusing on the importance of individualizing therapy. Emerging approaches such as anti-angiogenesis and other targeted therapies will be reviewed. Angiogenesis is central to cervical cancer development and progression. The dominant role of angiogenesis in cervical cancer seems to be directly related to HPV inhibition of p53 and stabilization of HIF-1 alpha both of which increase VEGF. The binding and inactivation of VEGF by bevacizumab seems to shrink cervical tumors and delay progression without appreciable toxicity and is being studied in a Gynecologic Oncology Group (GOG) phase III trial (protocol 0240). Other trials investigating the role of EGFR targeted agents have been disappointing. Indeed, mutations affecting the EGFR kinase domain in exons 18 through 21 appear to be absent. Finally, anti-HPV vaccines are intriguing.

[Figure 1]

References:


The advantages of robotic technology over laparoscopy (and laparotomy) have resulted in a rapid increase of radical hysterectomy, something it had not occurred with laparoscopy. The stereoscopic magnification provided by robotics has also facilitated the development of the nerve-sparing technique, with its advantages for a faster return of bladder function.

In a comparison study of the surgical approach at Mayo Clinic Arizona (1), robotics and laparoscopy were preferable to laparotomy due to lower blood loss and shorter hospitalization. The operating time was longer for the laparoscopy group and similar to laparotomy. There were no differences in intraoperative or postoperative complications among the three groups.

A subsequent study addressed the perioperative results of the nerve-sparing approach (2). A comparison of the conventional and nerve-sparing techniques revealed mean operating times of 225 vs 239 minutes, EBL 175 vs 135 ml, number of nodes 31 vs 24, and hospital days 1.6 vs 2, respectively. There were no intraoperative complications in either group, and postoperative complications were similar 22% vs 16% for the conventional and nerve-sparing technique.


Presidential Plenary: PRESIDENTIAL PLENARY: SURGERIES FOR INVASIVE CERVICAL CANCER PATIENTS - GLOBAL APPROACH

NERVE-SPARING LAPAROSCOPIC RADICAL HYSTERECTOMY

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Bladder dysfunction, colon motility impairment and sexual function disorder is a common surgical sequel of radical hysterectomy. Hypogastric nerve damage is a critical role of these dysfunctions. Since 1940 Dr. Okabayashi started to performed nerve sparing radical hysterectomy to preserved the nerve function and have a great success in maintain quality of life after radical hysterectomy. Up today more and more doctors underwent hypogastric nerve preservation radical hysterectomy in cervical cancer with tumor size within 2 cm. Most of the patients could remove Foley and have acceptable bladder function within 1 week after nerve sparing surgery. It is a safe and feasible procedure and more important it does not compromise the radicality.

However, high surgical technique and well understand the nerve anatomy of pelvis is very important in nerve sparing radial hysterectomy. It is the reason that the procedure is still not so popular in the world. Laparoscopic approach could provide a good surgical vision with a good hemostasis. It may decrease the learning cure of nerve sparing procedure.

To evaluate the procedure, international workshop and conferences for promoting the procedure is necessary and then prospective, randomize control trials could be performed. Finally, nerve sparing radical hysterectomy could be implemented as a standard treatment for cervical cancer patients.
Presidential Plenary: PRESIDENTIAL PLENARY: SURGERIES FOR INVASIVE CERVICAL CANCER PATIENTS - GLOBAL APPROACH

SELECTION OF EARLY CERVICAL CANCER PATIENTS FOR THE OKABAYASHI RADICAL HYSTERECTOMY, THE AMSTERDAM EXPERIENCE

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Introduction: Two controlled trials did not show a survival benefit for a more radical hysterectomy in early cervix cancer. The deliberate use of adjuvant radiotherapy in more than 50% of the patients in these studies confounded the conclusion that radicality does not matter. The Okabayashi variant of the radical hysterectomy represents one of the most radical variants especially where it concerns the dorsal paracolpal tissue. We performed a retrospective analysis of patients who had an Okabayashi technique analyzing loco regional control and survival.

Materials and methods: In 808 consecutive patients, clinical and pathological variables were analyzed and related to recurrence localization and survival. High and low risk subgroups were compared with similar groups from the literature. The data of a subgroup of consecutive patients with a minimum follow-up of 5 years were used in 12 existing prognostic models from the literature. The performance of the models was visualized in calibration plots.

Results: Loco regional recurrences in a high risk node negative Okabayashi group were lower compared with similar groups as published in the literature (8% versus 15% to 24% respectively). Central recurrence rate was 3%, while 24% of patients had adjuvant radiotherapy. Patients with positive lymph nodes showed a survival of 76%, comparing favourably with a reported survival of 51% to 81% from other large series. Stage IB2 patients had a 20% recurrence rate while 50% had adjuvant radiotherapy. When the data from the Okabayashi group were put into twelve published prognostic models, only 2 models were valid for the prediction of survival in our patient population, the other models underestimated survival.

Discussion and conclusion: It is suggested that a more radical hysterectomy results in decreased loco regional recurrences and better survival especially in high risk subgroups of early cervix cancer while it decreases the need for adjuvant radiotherapy. The morbidity of this strategy must be outweighed against the morbidity of a less radical approach with an increased need for adjuvant radiotherapy.
Presidential Plenary: PRESIDENTIAL PLENARY: SURGERIES FOR INVASIVE CERVICAL CANCER PATIENTS - GLOBAL APPROACH

RADICAL SURGERY IN PELVIC LYMPH NODE POSITIVE CERVICAL CANCER

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Introduction: With a completed 5 years follow up, we studied the outcome of LEP (laterally extended parametrectomy) operations, used in pelvic lymph node metastases cervical cancer.

Methods: In 70 out of 106 LEP-Wertheim operated patients, no adjuvant treatment was used. In 36 patients, where histology suggested tumor spread beyond the threshold of our surgery, adjuvant chemo-radiotherapy was advised. 5 years follow up was completed (without lost for follow up) for the whole cohort of patients.

Results: In 70 patients treated by LEP procedure alone, the overall 5-years survival was 91.4%. For those 36 patients, who were excluded due to disease spread above study criteria, 5 years survival was 44%. Complications in 10% of cases necessitated a second operation. Apart from transient hyper continence and one case of permanent incontinence, no severe quality of life consequence of the operation was observed.

Conclusions: Our results suggest that in 2/3rd of pelvic lymph node positive, stage IB cervical cancer cases surgery alone could provide equal or better survival (without the toxicity of chemo-radiotherapy), than any kind of multimodality treatment alternatives. LEP procedure should be considered a treatment option for stage IB cervical cancer patients with pelvic lymph node metastases.
WHAT IS RADICAL Hysterectomy?

S. Fujii

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As one of the surgical methods, Wertheim had introduced radical hysterectomy in 1911. Within the name of radical hysterectomy there was an important concept that the surgery should be radical enough for the extent of the disease for the treatment of invasive cervical cancers. Therefore, for more than 100 years, many doctors have been pursuing the ideal method of radical hysterectomy. This means that Wertheim's method was a mile stone for the development of ideal radical hysterectomy. However, if we may look the history of radical hysterectomy, the classification of radical hysterectomy introduced in 1974 has created the chaotic state in the surgeries named radical hysterectomy. Due to the vague anatomical description of their classification, completely different levels of surgeries named as radical hysterectomy were started to perform in all over the world. Consequently, under the different qualities of surgery, the surgical outcome had been discussed for the treatment of cervical cancer. However, recently, radical hysterectomy is going to be approached under the magnified surgical view by robotic machine, laparoscopic instruments or wearing loupe. The magnified surgical view is going to reveal the veil of the anatomical black boxes necessary for the radical hysterectomy and/or the improvement of the quality of life after the surgery. The time has come for us to discuss on “What is the ideal radical hysterectomy?” under the recent detailed surgical anatomy. Then, the time shall come for us to say that no need for us to classify radical hysterectomy. The most important goal to achieve is the high quality of surgical level for the treatment of cervical cancer. If we can define the ideal radical hysterectomy and perform the same quality of surgery, the patients in all over the world shall be satisfied with the outcome and the quality of life after the surgery.
NERVE-SPARING RADICAL HYSTERECTOMY AS TMMR: ROBOTIC

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The radical hysterectomy as total mesometrial resection (TMMR) in cervical cancer - firstly described by Michael Höckel - is different from other types of radical hysterectomies. It can be performed adequately on stage Ib, Ila and early IIb cervical cancer. The technique is based on ontogenetic anatomy and the presence of tumor permissive compartments. Thus, in contrary to the classical cancer surgery, not primarily width of tumor free margins is relevant, but complete removal of total permissive compartment of the primary tumor. In cervical cancer this corresponds to the "Müllerian compartment". Thus, removing the whole compartment (except for the distal vagina) and the downstream lymph basins, the bordering lamellae to adjacent compartments of bladder and rectum are kept intact and implicitly, the hypogastric plexus will be preserved. From the original data in open surgery it may be concluded that excellent locoregional control may be achieved by surgery alone, even when risk factors for recurrence are present. The author “translated” this technique from open to robotic surgery supported by M. Höckel. The principles of this technique and the differences with respect to other types of radical hysterectomies will be demonstrated. Short term outcome of “robotically assisted TMMR and therapeutic lymphadenectomy” will be reported.
Presidential Plenary: PRESIDENTIAL PLENARY: SURGERIES FOR INVASIVE CERVICAL CANCER PATIENTS - GLOBAL APPROACH

RADICAL HYSTERECTOMY

P. Benedetti Panici, I. Palaia, C. Marchetti, V. Di Donato, A. Musella, R.A. Besharat, L. Salerno, C. Bracchi, J. Caccetta, F. Bellati
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Radical hysterectomy represents the gold standard treatment in patients with early stage tumors and a valid choice of treatment, after neoadjuvant chemotherapies in locally advanced tumors. Since the first publications on radical hysterectomy many classifications, different approaches and techniques have been described and proposed in order to standardise and evaluate this type of treatment. Adaptation of radicality to tumour spread is an important topic in cervical cancer. On one hand, such adaptation has led to the development of ultraradical surgery; on the other hand, it has led to more-limited (i.e., modified radical) surgery based on the concept of the surgical margin and on the estimated risk of pericervical spread, knowing that cervical cancer can spread in any direction. As a result, the term “radical” or “extended” hysterectomy encompasses various types of surgery. During the last century, the classical Wertheim radical hysterectomy has undergone few changes. In the last years, an important effort has been made to establish a better standardization of the surgical procedure, to improve the definition of anatomic landmarks and to make comparison of procedures and outcomes possible. In 2008 Querleu-Morrow proposed a new classification of radical hysterectomy. The key strong points of the Querleu-Morrow classification (Q-M classification) include: the recognition of the extent of parametrial resection as the key and sole parameter for differentiation between types of radical hysterectomy; a unified terminology; the use of anatomical landmarks to classify parametrial resection and the inclusion of a nerve-sparing modification of radical hysterectomy. The Q-M classification system, however, does not include a description of parametrial resection in three dimensions, which is a significant topic that requires further clarification, particularly in the most frequent types of the procedure, i.e., types C1 and C2. For this reason more recently a revision of the Q-M classification has been done defining precisely parametrial resection on a three-dimensional anatomical template, including nerve sparing procedure. It has been made by an international committe with the aim of better standardization (including nomenclature) of the radical hysterectomy, enhancing harmonization of clinical practice in gynecological oncology.
Interactive Session: I CAN’T BELIEVE THEY DID THAT THROUGH THE SCOPE!

CONTROL OF MAJOR ARTERIAL INJURY

M.M. Leitao

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Video will be presented to demonstrate control of a major arterial injury using the robotic platform. A 48-year-old woman with a BMI of 38 presented with stage IB1 cervical cancer. Robotic-assisted radical hysterectomy, BSO, sentinel lymph node mapping followed by complete PLND and para-aortic lymph node sampling was performed using the da Vinci® Si System. When proceeding to right-sided PLND, the surgeon activated the scissors’ monopolar coagulation-type current, set at 35 W. A spark travelled through the protective sheath, creating a hole in the right external iliac artery. The artery was grasped with a Cadiere forceps to tamponade bleeding, and the defect was sutured robotically with a 5.0 Prolene interrupted stitch. EBL was 250cc and laparotomy was not required. The patient had an uncomplicated postoperative course and was discharged home 2 days after surgery without any subsequent sequelae.
Interactive Session: I CAN’T BELIEVE THEY DID THAT THROUGH THE SCOPE!

REPAIR OF LARGE VESSEL INJURY DURING MIS

A. Moussa, S. Lau, J. Press, S. Brin, W. Gotlieb

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Large vessel injury is more prone to occur during MIS for gynecologic malignancies in view of the distortion of the anatomy, difficult exposure, radicality of surgery, previous pelvic surgery, and/or prior radiotherapy. Iatrogenic injuries of high flow, low pressure veins are associated with high morbidity (50%) and death resulting from uncontrollable bleeding, coagulopathy, and multisystem organ failure occurs in up to 18% of cases. The most important intervention is to acutely occlude the bleeding in order to interrupt the blood loss and obtain good exposure of the trauma. Pressure applied on the bleeder is performed first, followed sometimes by clamping the vessel. Updating the anesthesia team and ordering replacement fluids is imperative in the first moments following the event. One should avoid to blindly suture, clamp, or cauterize the area. Prolonged pressure including hemostatic chemicals can be attempted and is sometimes therapeutic in view of the low venous pressure. Hemoclips can be used for easily accessible small defects. Bovine pericard patches and overlay autogenous tissue (OAT) have been utilized with success in large defects that cannot be controlled by suturing only. One should never hesitate to call for support from other team members. Open packing is sometimes necessary in diffuse uncontrollable bleeding to allow the patient to recover from acidosis, hypothermia and coagulopathy. Following recovery of the acute event, prevention of blood clot formation is indicated.
Interactive Session: I CAN’T BELIEVE THEY DID THAT THROUGH THE SCOPE!

THE PROCESS OF TRANSFORMING OPEN PELVIC EXENTERATION TO A TRUE MINIMALLY INVASIVE APPROACH USING THE DAVINCI® ROBOTIC DEVICE

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Objective: The purpose of this discussion is to demonstrate the process of developing the technique as well as the successful adaptation of radical pelvic surgery for removal of advanced gynecologic malignancies. These cases have been traditionally performed through an open abdominal incision, now we propose performing them utilizing minimally invasive robotic technology.

Materials: In the past few years, our Gynecologic Oncology service has attempted to incorporate the use of the daVinci® Robotic platform into a broad range of surgical procedures. The philosophy has been to convert as many open procedures as possible to a "closed space" using a minimally invasive approach with the daVinci®, thereby employing the often lauded surgical advantages of the technology. Between May 31, 2007 and April 5, 2012 we offered a robotic approach for pelvic exenteration to 12 consecutive patients who presented with advanced pelvic malignancy.

Results: During the study period, 12 consecutive patients were taken to the operating room with the intention of performing an anterior, posterior or total pelvic exenteration. We were able to complete seven successfully with the robotic approach without conversion to open, including 5 out of the last 7 cases. In addition, we have been able to complete 4 consecutive intracorporeal ileal conduits for urinary diversion using the robotic technique. We had a very diverse group of patients with no preselection criteria. Mean age was 63.3 years (43-76) and mean BMI was 31.6 (19.6-52.1). Mean operative time was 515 minutes and mean LOS was 11.3 days (range 4.0 - 28.0). There were no perioperative deaths.

Conclusions: As we begin to use the daVinci® Robotic platform more for a variety of surgical procedures, it is important to be able to demonstrate feasibility of accomplishing these procedures through this minimally invasive approach. However it is also incumbent on the early adopters to report all outcomes in order to accumulate collective data regarding successes, failures and any patient safety issues. We must also be able to describe the procedure systematically and in detail in order to validate a given approach through reproducibility across a variety of clinical settings.
Interactive Session: MANAGEMENT OF HIGH RISK GTN AND PSTT/ETT

SALVAGE THERAPIES FOR THE MANAGEMENT OF METASTATIC HIGH-RISK GESTATIONAL TROPHOBLASTIC NEOPLASIA (GTN)

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Objective: Approximately 40-50% of patients with FIGO-defined metastatic high-risk GTN will have an incomplete response to first-line multiagent EMA-CO chemotherapy or will relapse from remission. Our objective was to assess the value of salvage therapy, including chemotherapy, surgery and radiation, in the management of metastatic high-risk GTN after failure of initial multiagent chemotherapy.

Materials and methods: Forty-nine women with metastatic high-risk GTN received treatment at the Brewer Trophoblastic Disease Center between 1986 and 2010. Patients who had incomplete responses or developed resistance to EMA-CO chemotherapy were treated with drug combinations employing etoposide and a platinum agent with methotrexate and actinomycin D (EMA-EP), bleomycin (BEP), ifosfamide (VIP, ICE), or paclitaxel (TP/TE). Adjuvant surgery and brain irradiation were used in selected patients. Clinical response and survival as well as factors effecting outcomes were analyzed retrospectively.

Results: Twenty-eight (57%) of 49 high-risk patients developed resistance to EMA-CO, including 13 (46%) of 29 patients treated primarily. Twenty-three patients (82%) had lasting complete responses to EMA-EP (9), BEP (9), VIP (1), ICE (3), or TP/TE (1). Brain irradiation was given to 4 patients who developed brain metastases during treatment, 3 of whom survived. Operative procedures were performed to remove resistant foci of disease in the lungs (9) or uterus (2) in 11 (39%) of the 28 patients, 9 (82%) of whom survived. Survival was significantly influenced by hCG level at the start of salvage therapy (p < .001), number of metastatic sites (p < .02), and metastases to sites other than the lung and vagina (p < .05).

Conclusions: Salvage therapy with platinum/etoposide-based drug regimens, often in conjunction with surgery and brain irradiation, was successful in achieving cure in 82% of 28 high-risk GTN patients who failed EMA-CO chemotherapy and was ultimately responsible for survival in 53% of the 43 high-risk GTN patients who were cured.
Interactive Session: SECONDARY CYTOREDUCTION IN OVARIAN CANCER (DEBATE)

BEST CHEMOTHERAPY AFTER SECONDARY SURGERY

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There are no data that show that chemotherapy after secondary cyto-reductive surgery is of any benefit and there have been no randomised trials that compare different regimens in this situation. Recommendations can therefore only be viewed as guidance and such guidance is based on inference and assumptions. The 3 main assumptions are:

1. Patients who received secondary cyto-reductive surgery are patients with platinum-sensitive disease

2. Chemo-sensitive disease is best treated by combination platinum-based therapy

3. Secondary cyto-reduction is associated with residual microscopic disease and therefore without follow up ‘adjuvant’ chemotherapy relapse is inevitable.

Thus, logic would dictate that after secondary cyto-reductive surgery patients should be treated with a platinum-based combination such as carboplatin + gemcitabine, carboplatin + liposomal doxorubicin or a re-challenge with carboplatin + paclitaxel.

One option for patients who have secondary cyto-reduction might be observation only. There are data that support this strategy and they relate to the now well established fact that there is no benefit to chemotherapy early in a relapse. It is well recognised that a CA125 rises 3-6 months prior to gross disease being present on the CT or symptoms being experienced, and this paradigm has echoes in the clinical scenario post secondary cyto-reduction i.e. minimal disease is present.

Therefore before secondary cyto-reductive surgery takes place, consideration needs to be given to the pace of disease and treatment-free interval. Patients who relapse between 6 and 12 months do not have a particularly good prognosis and most most would recommend chemotherapy post surgery, indeed one could argue that surgery should not go ahead unless post-operative chemotherapy will be given. For patients who relapse late, particularly if there is only a single site of disease, serious consideration should be given to observing the patient and not automatically giving post-operative adjuvant chemotherapy.
Interactive Session: SHOULD ALL OVARIAN CANCER PATIENTS UNDERGO BRCA MUTATION TESTING?

SHOULD ALL OVARIAN CANCER PATIENTS UNDERGO BRCA MUTATION TESTING?

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“An ounce of prevention is worth a pound of cure”

Benjamin Franklin (1706-1790)

In the struggle against ovarian cancer it seems that population screening, radical cytoreductive surgery and aggressive chemotherapy are unable to make a significant impact on the high mortality rate from this malignant disease.

However, significant data has accumulated over the past decade, demonstrating a major effect of Oral Contraceptive use as well as Risk Reducing Surgery (RR-BSO) on the overall mortality from ovarian cancer in normal and high risk individuals.

In addition, evidence from multiple analyses confirms the presence of hereditary cancer in about 10% of all ovarian cancer patients.

It is therefore quite obvious, that if economically reasonable and medically safe, testing for mutations in BRCA1/2 in ovarian cancer patients can disclose a large population of family members who are at significant risk (40%-70%, life time) for which preventive measures are highly effective and acceptable.

In our population of Ovarian Cancer patients, close to 40% belong to the Ashkenazi Jewish ethnic group of which 2.5% are carriers of one of three common founder mutations in BRCA1/2. Therefore, we have adopted the policy of testing all our ovarian cancer patients for these mutations, regardless of family history.

This approach has been very important to female relatives of our patients who were found to be carriers as a result of this testing policy. While the costs are reasonable, and false positive results non-existent, women can plan preventive measures such as prolonged OC use, risk reducing surgery, family planning and Pre-Gestational Diagnosis (PGD).

In the setting of non high risk population, the issue is more complicated and the reasons for doubt of efficacy stem from two main problems: a) the cost of sequencing the two main genes is very expensive at the present time, and b) the sequencing might reveal many variants of undetermined significance (VUS).

It is our impression that in the era of personalized medicine this practice will prevail.
Interactive Session: THE PROPER MANAGEMENT OF EARLY STAGE ENDOMETRIAL CANCER IS... (DEBATE)

THE INCREASING CREDIBILITY OF SENTINEL NODE MAPPING (SLN) IN ENDOMETRIAL CANCER STAGING

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Introduction: Most gynecologic oncologists would agree that a main objective of regional lymphadenectomy for endometrial cancer staging is the detection of microscopic lymphatic spread that would allow appropriate adjuvant therapy to be administered which may substantially increase the cure rate in these select cases. There is increasing evidence that sentinel node mapping of clinical stage I endometrial cancer is feasible via a simple cervical injection at the time of exam under anesthesia.

A prospective database of all patients who underwent SLN mapping for endometrial cancer was reviewed. Cervical injection of blue dye was used in all cases. The surgical algorithm is as follows: 1) peritoneal and serosal evaluation and washings; 2) retroperitoneal evaluation including excision of all mapped SLNs and suspicious nodes regardless of mapping; 3) if there is no mapping on a hemipelvis, a side-specific pelvic, common iliac, and interiliac lymph node dissection (LND) is performed. Paraaortic LND is performed at the attendings’ discretion. The algorithm was retrospectively applied.

Results: From 9/2005-4/2011, 498 patients received a blue dye cervical injection for SLN mapping. At least one LN was removed in 95% of cases (474/498); at least one SLN was identified in 81% (401/498). SLN correctly diagnosed 40/47 patients with nodal metastases who had at least one SLN mapped, resulting in a 15% false-negative rate. After applying the algorithm, the false-negative rate dropped to 2%. Only one patient, whose LN spread would not have been caught by the algorithm, had an isolated positive right paraaortic LN with a negative ipsilateral SLN and pelvic LND.

Conclusions: Satisfactory SLN mapping in endometrial cancer requires adherence to a surgical SLN algorithm and goes beyond just the removal of blue SLNs. Removal of any suspicious node along with side-specific lymphadenectomy for failed mapping are an integral part of this algorithm.
Interactive Session: THE PROPER MANAGEMENT OF EARLY STAGE ENDOMETRIAL CANCER IS… (DEBATE)

THE ROLE OF ROBOTIC SURGERY IN WOMEN WITH ENDOMETRIAL CANCER

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Most women with endometrial cancer (EC) present with apparent early stage disease and will be managed surgically. The overall management of patients with apparent early stage EC continues to evolve. EC remains the least uniformly managed gynecologic malignancy, even amongst gynecologic oncologists. There exists a great deal of debate regarding the route of surgical approach, whether the patient should undergo comprehensive surgical staging, and the extent of the lymph node dissection.

Approximately 15-25% of these patients, with apparent early disease, will be upstaged as a result of surgical staging. The majority of patients with EC discovered with extra-uterine disease have occult metastases. Current disease assessment modalities such as pre-operative imaging, intra-operative palpation, gross inspection and frozen section of the uterus all are inaccurate when compared to comprehensive surgical staging that includes bilateral pelvic and para-aortic lymph node dissection. Comprehensive surgical staging with lymphadenectomy provides the best definition of the biologic nature of the disease and allows the gynecologic oncologist to make informed postoperative treatment decisions, which will minimize the need for adjuvant therapy in those patients with early-stage EC and allow for implement offering curative therapy to those with extra-uterine disease.

A hysterectomy-BSO and comprehensive pelvic and para-aortic lymph node dissection can be accomplished via laparotomy or minimally invasive surgery (MIS), which includes laparoscopy (LS) and the robotic platform. The majority of women with presenting with EC are obese, elderly and/or suffer from multiple co-morbidities. These patients should be offered an MIS approach in order to improve peri-operative outcomes. While advanced LS technology has been available for over two decades, the incorporation of MIS into surgical management of the gynecologic oncology patient has been relatively slow. Whether this relative lack of mainstream adaptation of LS into the practice is due to technology or training limitations is unclear although strong biases support both potential causes. While difficult to quantify, there is a long and difficult learning curve related to LS pelvic and para-aortic lymphadenectomy, which has limited the use of MIS in the surgical management of EC.

Robotic surgery overcomes many of the technologic limitations of LS. The robotic platform provides the surgeon superior high definition 3-D vision, magnification, wristed instruments and motion scaling. These significant technological improvements have allowed the gynecologic surgeon to perform much more complicated surgeries via MIS on a heterogeneous group of patients. Therefore, in order to optimize surgical outcomes and accurately direct post-operative management, women presenting with apparent early-stage EC should undergo robotic hysterectomy-BSO with pelvic and para-aortic dissection.
Interactive Session: TREATMENT FOR STAGE IIB CERVICAL CANCER: CURRENT AND FUTURE PERSPECTIVE

DOES CONFORMAL RADIATION IMPROVE THE SURVIVAL AND QOL IN LOCALLY ADVANCED CERVICAL CANCER?

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Chemoradiation is the state of the art treatment for advanced cervical cancer patients. Chemotherapy significantly improved overall survival rates from about 50 to 60 %, leaving still space for optimizing the treatment approaches. Cervical cancer is a challenging tumor site for radiation therapy. Treatment targets consist of the primary tumor, affected nodes and the surrounding tissues being at risk for microscopic disease. All target volumes move inside the pelvis along with the movements and volume changes of the unaffected organs and tissues. Additionally, cervical cancers can shrink during the course of treatment, resulting in individual tumor reductions and deformations. The challenging part of radiotherapy nowadays is to tailor the dose to the changing targets and to keep it away from the healthy surrounding and the advantages of image guided adaptive radiotherapy (IGART) strategies are widely investigated in this respect. The goal is to increase the therapeutic window, with a better chance on tumor control, reduced morbidity and a better quality of life. 3-D imaging technology and especially MRI information played an essential role in the developments of modern brachytherapy approaches. It allowed movement from point to volume based related dosimetry (resulting in European and American guidelines) and to the adaptation of traditional applicators. Currently the gain of IGART is widely explored (1) and several publications demonstrate a clear dosimetric benefit over standard approaches. But there is also evidence coming up that improved dosimetry translates into clinical gain. IGART consisting of 3-D conformal treatment or IMRT together with MRI guided adaptive brachytherapy seems to improve local control and survival rates and reduces morbidity compared to historical series. In the Vienna series (2) for example, local control in FIGO IIB cancers was achievable in about 95% of the patients with a 3-year actuarial cancer specific survival rate of 84%.
Interactive Session: TREATMENT FOR STAGE IIB CERVICAL CANCER: CURRENT AND FUTURE PERSPECTIVE

PERSPECTIVE OF RADICAL SURGERY FOLLOWING NEOADJUVANT CHEMOTHERAPY (NAC) OR CHEMORADIOThERAPY (CCRT)

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In the past decade, 5 randomized clinical trials have demonstrated an advantage in terms of disease-free (DFS) and overall survival (OS) for locally advanced cervical cancer (LACC) patients treated with concomitant radiation and cisplatin-based chemotherapy compared with respect to exclusive radiotherapy, so that it currently represents the gold standard in the treatment of these patients. On the other hand, different experiences from Europe and South America have shown a comparable absolute benefit of 15% at 5-year survival, using neoadjuvant chemotherapy followed by radical surgery in the same group of cases. Nevertheless, the 5-year survival of LACC patients is around 70%, hence other therapeutic approaches have been tested to further improve prognosis. In this context, the possibility to combine strategies to maximize local control and improving quality of life should be considered. Among different approaches, the use of a three-modality treatment, including radiotherapy, chemotherapy and surgery, has been actively investigated. With a median follow-up of 58 months, we observed in a consecutive series of 174 cases submitted to CT/RT followed by radical surgery a complete/microscopic pathological response in 124 patients (71.3%). 5-year DFS was 75.5%, while the 5-year OS was 77.4%. In multivariate analysis, residual tumor and stage of disease were the powerful prognostic factors for DFS and OS. As far as long-term toxicity is concerned, 8 out of 22 complications were grade 3/4. We recently analyzed also the role of obesity in administering CT/RT to LACC patients, showing the absence of differences according to BMI levels in intraoperative and postoperative complications; moreover, this tri-modal approach has been also demonstrated to be safe in patients with moderate/severe comorbidities. Focusing on QoL issues, our 2-year prospective longitudinal analysis has shown in LACC patients receiving CT/RT, QoL scores comparable to those achieved by early stage cervical cancer patients treated with radical surgery alone, with lymphedema and menopausal symptoms as the most disabling treatment-related sequelae. Taken together these data confirm the feasibility and efficacy of CT/RT in the treatment of LACC patients, but more efforts will be required in the next future to adequately address the clinical and psychosocial unmet needs of these patients.
Interactive Session: TREATMENT FOR STAGE IIB CERVICAL CANCER: CURRENT AND FUTURE PERSPECTIVE

ROLE OF RADICAL HYSTERECTOMY IN STAGE IIB CERVICAL CANCER: PRIMARY OR NEOADJUVANT CHEMOTHERAPY (NAC) SETTING

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Radical hysterectomy with postoperative radiation therapy (RT) has been standard treatment for Stage IIB cervical cancer in European and Asian countries including Japan. In such primary surgery series, parametrial involvement was reportedly proven in 34-85% (41%, Kyoto [n=144]), lymphnode metastasis was present in 39-56% (42%), and 5-year survival rate varied 64-78% (69%). Due to recently recognized limitation of concurrent chemoradiation therapy (CCRT) for survival improvement and quality of life (QOL), neoadjuvant chemotherapy (NAC) followed by surgical resection of resistant cancer cells has received much attention. Meta-analysis also showed that, being compared with primary surgery, NAC plus surgery may be beneficial for improvement of recurrence-free survival but not of overall survival.

In our institution, we started NAC using platinum-based multidrug regimen in 1990. To minimize the late complications, we abandoned postoperative RT in 1999. Currently, we give 2 cycles of NAC with platinum plus irinotecan (#JOG1065), perform Okabayashi's radical hysterectomy, and then add 4 cycles of adjuvant chemotherapy. Radical surgery following NAC was feasible in all of Stage IIB patients (n=67). Toxicities were acceptable, and CR/PR was obtained in 82%. Parametrial involvement and lymphnode metastasis was seen in 42% and 43%, respectively. Overall 5-year survival rate was 80%. There were no severe late complications in the group without postoperative RT, in contrast to high incidence of lymphedema or intestinal complications in the RT group.

In conclusion, combination of surgery and chemotherapy is the promising modality for patients with Stage IIB cervical cancer for improvement of QOL of patients. NAC followed by surgery should be compared with CCRT in the randomized trials.
Interactive Session: WHAT THE HECK IS HIPEC AND HOW DO YOU GIVE IT?

HIPEC - HOW TO GET STARTED

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Hyperthermic intra-operative intraperitoneal chemotherapy (HIPEC) following surgical cytoreduction is at the cutting edge of treatment and still quasi-experimental for advanced ovarian or peritoneal carcinoma. Like peritonectomy, it is a treatment modality with significant risks and when combined with peritonectomy carries significant morbidity and mortality risks. The single biggest controllable determinate of survival in advanced ovarian or peritoneal carcinoma, is the completeness of cytoreduction. If you cannot obtain complete/optimal cytoreduction, defined as no visible post-surgical residual disease, then you are not ready to start using HIPEC.

To work at the cutting edge of treatment doing peritonectomy and HIPEC requires attention to detail at all levels. The most important aspects are firstly good patient selection and secondly management by a team who are all capable of carrying out their roles to the highest standard. There is no place for shortcuts in these processes. The team involves all levels of hospital support and involvement from the hospital’s administration, through to medical, nursing, allied health, pharmacy and laboratory backup is required.

It should be remembered that just because you can do an operation or procedure doesn’t mean you should do that operation or procedure. All patients should have detailed workup prior to being accepted for peritonectomy and HIPEC. Our patients have a range of blood tests, echocardiogram, respiratory function tests including gas exchange and exclusion of extraperitoneal disease. When these are completed they are seen by the key medical members (oncology surgeon, anaesthetist, intensivist and medical oncologist). Each case is discussed by this team and if there are any concerns which cannot be resolved then the patient will not be accepted for peritonectomy and HIPEC.
Interactive Session: WHAT'S CLEAR AND NOT CLEAR ABOUT CLEAR CELL CANCER

NEW JGOG TRIAL CONCEPT FOR RECURRENT CLEAR CELL CARCINOMA OF THE OVARY (EVEROCC PHASE II TRIAL)

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Number of basic studies have suggested that PI3K-Akt-mTOR pathway is highly activated in clear cell adenocarcinoma(CCC) than in other histological types of ovarian carcinoma, and mTOR inhibitors may improve the prognosis of patients with CCC. Currently, there is no effective standard chemotherapy for recurrent ovarian CCC. Therefore, the Japan Gynecological Oncology Group (JGOG) planned a Phase II study (Everolimus in Patients With Recurrent Ovarian Clear cell carcinoma: EVEROCC trial) to evaluate the efficacy of everolimus, an mTOR inhibitor, for recurrent CCC.

The primary endpoint is the disease control rate (CR + PR + SD for ≥8 weeks), and secondary endpoints include overall survival, progression-free survival, and adverse events. Protocol treatment is oral everolimus at 10 mg/day (28 days per cycle), which is continued until disease progression or unacceptable adverse events occur. Eligible patients have

1) recurrence after at least one platinum-containing anticancer regimen,

2) an evaluable lesion at enrollment that can be repeatedly measured, and

3) receive the study regimen as 2nd-line or 3rd-line treatment.

To assess the response, target and non-target lesions are evaluated by CT or MRI before and after starting treatment according to RECIST1.1. Adverse events are evaluated using NCI-CTCAE ver.4.0. The planned number of patients is 50 and the study duration is four years (2 year enrollment and 2 year observation). Translational research will be incorporated to identify biomarkers for predicting the therapeutic effect of everolimus. To the best of our knowledge, this is the first clinical study assessing monotherapy with an mTOR inhibitor (everolimus) in patients with recurrent ovarian CCC. It is also the first investigator-initiated registration-directed clinical trial with a molecular targeting drug conducted by JGOG.
Interactive Session: WHAT'S CLEAR AND NOT CLEAR ABOUT CLEAR CELL CANCER

MOLECULAR ISSUE
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Clear cell carcinoma (CCC) of the ovary is biologically distinct entity, different from other epithelial ovarian cancer. CCCs are characterized by its association with endometriosis or deep venous thrombosis. When compared with more common high-grade serous adenocarcinomas (HGSC), patients with CCC have a poorer sensitivity to platinum-based chemotherapy and a worse prognosis. However, the genetic or molecular alterations responsible for these unique features of CCC have been fully understood.

It has been recently reported that CCCs are associated with frequent mutations in ARID1A and PIK3CA. The frequency of ARID1A and PIK3CA gene mutations are reported to be roughly 50% and 40%, respectively. ARID1A, a tumor suppressor gene, encodes BAF250A. The loss of BAF250A expression in CCCs has been frequently observed in ovarian CCCs, however, the molecular events mediated by the loss of BAF250A expression remain unclear. Among the molecular targets, PI3K-AKT-mTOR signaling pathway seems to be the most promising. The activating mutations in PIK3CA observed in CCCs theoretically result in the activation of this signaling pathway. The recent investigations showed that mTORC1 is more frequently activated in ovarian CCCs than in HGSCs, and can be a therapeutic target. In contrast to mTORC1, the activation of mTORC2 in CCCs and its role as a therapeutic target are yet to be determined. Currently, the phase II clinical studies of mTORC1 inhibitors in the setting of monotherapy or in combination with chemotherapy are being investigated in patients with ovarian CCC. Mutations or amplifications in HNF1B, PPM1D, or PPP2R1A, loss of PTEN expression, overexpression of HIF-1a or VEGF have also been observed in ovarian CCC, and their role as a therapeutic target are currently being investigated. Review of these preclinical data and the scientific rationale for the use of novel targeted agents in the treatment of ovarian CCC will be presented.
Interactive Session: WHAT'S CLEAR AND NOT CLEAR ABOUT CLEAR CELL CANCER

CURRENT COOPERATIVE GROUP CLINICAL TRIALS IN CLEAR CELL CARCINOMA OF THE OVARY

J. Farley

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Ovarian clear cell carcinoma (OCCC) is a rare histologic subtype of epithelial ovarian cancer (EOC) that exhibits a distinct clinical and molecular behavior when compared with other histologic subtypes. Despite their tendency to present at an earlier stage, OCCCs often display poor prognostic behavior.

In a study of similarly treated advanced EOC patients, clear cell tumors had a decreased median overall survival of 24 months compared to 45 and 56 months for serous and endometrioid histologies, respectively. The biologic basis of this poor prognosis is thought to be secondary to OCCC's high chemoresistance to conventional platinum-based chemotherapy. Prior studies have documented a mere 11-29% response rate in OCCC compared to the approximate 70% response rate observed with papillary serous tumors. There are currently three cooperative group clinical trials available specifically targeting OCCC.

The aim of this review is to summarize the recent ongoing or planned cooperative group clinical trials in OCCC and any advancement in the treatment of this disease.
State of the Art TAXONOMY OF GYNECOLOGIC CANCERS

GENOMIC CHARACTERIZATION OF HIGH GRADE SEROUS OVARIAN CANCER BY THE CANCER GENOME ATLAS (TCGA) PROJECT

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High grade serous ovarian cancer accounts for about 60% of epithelial ovarian cancers and is responsible for most deaths. A catalogue of molecular aberrations that cause ovarian cancer is critical for developing and deploying therapies that will improve survival as well as for developing early detection and prevention approaches. The Cancer Genome Atlas (TCGA) project analyzed messenger RNA expression, microRNA expression, promoter methylation and DNA copy number in 489 high-grade serous ovarian adenocarcinomas and the DNA sequences of exons from coding genes in 316 high grade serous ovarian cancers (Nature 2011;474:609). High-grade serous ovarian cancer is characterized by TP53 mutations in almost all cases (96%); low prevalence but statistically recurrent somatic mutations in nine further genes including BRCA1, BRCA2, RB1, NF1 and CDK12; 113 significant focal DNA copy number aberrations; and promoter methylation events involving 168 genes. Analyses delineated four ovarian cancer transcriptional subtypes (mesenchymal, proliferative, immunoreactive and differentiated), three microRNA subtypes, four promoter methylation subtypes and a transcriptional signature associated with survival duration, and shed new light on the impact that tumors with BRCA1/2 and CCNE1 aberrations have on survival. Pathway analyses suggested that homologous recombination repair of DNA damage is defective in about half of the cancers analyzed, and that NOTCH and FOXM1 signaling are involved in serous ovarian cancer pathophysiology. The TCGA data are publically available to the research community online and serve as an invaluable resource for the development of new strategies that aim to decrease the impact of this disease in women.
Meet the Professor "PLATINUM RESISTANT" OVARIAN CANCER - A CLINICAL MINEFIELD! WHAT IS IT, WHO TO TREAT AND HOW TO MEASURE BENEFIT?

M. Friedlander, A. Tinker

Platinum sensitivity/resistance is a continuum and is not simply related to arbitrary time points, therefore it cannot be predicted by progression-free interval (PFI) alone. Despite an improved understanding of the complex interplay between clonal selection and the microenvironment of resistant tumours there is much to learn about the mechanisms of platinum resistance. The variable outcomes in patients with "platinum-resistant" ovarian cancer may be related to the heterogeneity of patients enrolled in clinical trials, the differing definitions of recurrence and probably also to the underlying mechanisms of resistance. Timing of treatment (symptomatic vs. asymptomatic) as well as number of lines of prior therapy and factors such as BRCA mutation status, and histologic subtype raise questions about how best to define platinum resistance and have implications for clinical practice. PFI is dependent on the frequency and nature of investigations obtained during follow up. The GCIG consensus was that trials should specify how PFI was defined i.e., CA125 alone, radiological or symptomatic recurrence, given that each subset may be quite different with respect to prognosis and likelihood of response. The consensus also recommended categorising patients according to the platinum free interval rather than make assumptions regarding likelihood of response to platinum. This has important implications for trial design. The aim of treatment of patients with "platinum resistant" ovarian cancer is symptom control and delaying symptomatic progression. Patients entered onto clinical trials are not necessarily representative of patients in the clinic and the results of clinical trials may not be applicable to all patients. For example in Stage 1 of the Symptom Benefit Study 40 % of patients progressed within 2 cycles of treatment arguing for improved selection criteria. The impact of treatment on symptom control remains uncertain and there is an international effort underway to develop better tools to measure benefit of treatment.
Meet the Professor ADVANCES IN PELVIC RECONSTRUCTION FOLLOWING RADICAL SURGERY

ADVANCES IN PELVIC RECONSTRUCTION FOLLOWING RADICAL SURGERY

B. Lampe

Florence-Nightingale Krankenhaus, Duesseldorf, Germany

Advances in reconstructive cancer surgery of the pelvis can improve quality of life in curative or palliative situations. Requirements and operative techniques for reconstructing functional organs will be illustrated and discussed. Different state of the art procedures for vaginal and bladder augmentation and reconstruction will be presented. The anatomic basis of reconstruction will be particularly emphasized as well as the management of surgical complications related to these operations.
Meet the Professor CANCER IN PREGNANCY

LONG TERM OUTCOME OF CHILDREN AFTER ANTENATAL EXPOSURE TO CHEMOTHERAPY

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Background: While oncologic treatment of maternal cancer during pregnancy has become more acceptable in the last decade, the effect of prenatal exposure to chemotherapy on cardiac and neurodevelopmental outcomes of the offspring remains uncertain. We aim to document general health, cardiac function and neurodevelopmental outcome in children who were prenatally exposed to chemotherapy. Our first analysis of a prospective multicentre study is presented.

Methods: Children were examined at birth, at the age of 18 months, 6, 9, 12, 15 and 18 years. The tests comprised a clinical neurologic examination, testing of the general level of cognitive functioning (Bayley/IQ-test), an electro- and echocardiography and questionnaire on general health and development. From the age of five years, also an audiometry, AVLT, CMS and Tea-Ch were performed and the CBCL was completed.

Findings: In total, 236 cycles of chemotherapy were administered in 68 pregnancies. Seventy children, born at a median gestational age of 35.7 weeks (range, 28.3-41.0; 47/70 < 37weeks), were included with a median follow-up period of 22.3 months (range, 16.8 -211.6). Although neurocognitive outcomes were within normal ranges, the high incidence of preterm birth had a negative influence on cognitive development. Children's behaviour, general health, hearing and growth were reported as in a general population. A severe neurodevelopmental delay was seen in both members of a twin (3%). Cardiac dimensions and functions were within normal ranges.

Interpretation: Fetal exposure to chemotherapy was not associated with increased morbidity at the level of the central nervous system, cardiac, and auditory functions, as well as general health and growth. More subtle changes in cardiac and neurocognitive measurements emphasize the need for longer follow up. Prematurity was frequently encountered, and was associated with impairment in cognitive development. Therefore, iatrogenic preterm delivery should be avoided as much as possible.
Meet the Professor CANCER IN PREGNANCY

BREAST CANCER IN PREGNANCY

F. Amant

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Breast cancer in pregnancy is uncommon though not rare. Breast cancer staging and treatment can be performed during pregnancy and is preferably discussed and executed in a centre with sufficient expertise. A staging and subsequent treatment strategy, should be defined in a multidisciplinary setting. Tumour biology, stage and gestational age at diagnosis determine the approach. Breast cancer surgery is possible during all trimesters of pregnancy. The distance to a small volume pregnant uterus renders breast radiotherapy possible during the first and second trimester, but not during the third trimester. New insights add to the practice to administer chemotherapy from 14 weeks gestational age onwards. The state-of-the-art of breast cancer treatment applies to pregnant breast cancer patients, but tamoxifen and trastuzumab are contraindicated during pregnancy. Since the long term consequences of prematurity are a concern, it should be prevented whenever possible. Cancer treatment during pregnancy will decrease the need for early delivery and thus prematurity.
Meet the Professor FERTILITY SPARING OPTIONS IN EARLY STAGE CERVICAL CANCER

THE ROLE OF ULTRACONSservative SURGERY IN EARLY CERVICAL CANCER

J.H. Shepherd

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Traditional assessment and staging of cervical cancer is by clinical examination followed by microscopy of the histopathology. Measurement of depth of invasion and diameter of the tumour determines the stage and has dictated treatment.

Earlier detection of disease and more precise imaging with a better understanding of the natural history has encouraged the development of a more conservative fertility-sparing approach. Colposcopy directs accurate biopsies so that once the diagnosis is established the size, volume and position of the tumour may be visualized by endo-vaginal MR imaging. The feasibility of fertility sparing surgery by trachelectomy or cone biopsy is assessed. Microscopy of the biopsy specimen determines the need for pelvic node assessment depending on the presence of LVSI as well as the depth of invasion. Imaging of the pelvis by CT or MRI will identify any suspicious lymphadenopathy. Sentinel node techniques will aid identifying node positive patients or those at particular risk.

The development of radical trachelectomy techniques has shown that conservation of the corpus uteri is not only possible but allows future successful fertility and good cure rates. Careful selection is the key with small early stage tumours. Of the 230 cases from the authors institution over 50% had no remaining or residual invasive disease. This is confirmed by the 1000 (approximately) cases of RVT reported world wide. Experience with the abdominal procedure is less.

Equally important is a realistic assessment of the woman’s fertility prospects and wishes taking into account fecundity, age, gynaecological pathology and medical co-morbidities as well as social circumstances. Individualization with a realistic analysis is the key to making a decision.

Treatment therefore will range from conisation to radical hysterectomy and pelvic node dissection. Dissected cone buicpsy with or without PND is adequate treatment in a significant number of selected patients with early stage invasive disease.
Meet the Professor FERTILITY SPARING OPTIONS IN EARLY STAGE CERVICAL CANCER

THE ROLE OF NEOADJUVANT CHEMOTHERAPY IN LARGER IB1 LESIONS (> 2 CM)

A. Maneo

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Introduction: The oncological results of fertility-sparing surgery in cervical cancers larger than 2 cm are unsatisfactory. Currently, only tumors smaller than 2 cm are admitted to radical trachelectomy. The tumor volume reduction after neoadjuvant chemotherapy (NACT) broadens the inclusion criteria for preservation of fertility and allows for a less radical removal of the cervical stroma, thus improving the chance for successful pregnancy.

Material and methods: Since 2006 to May 2012 ten original reports about NACT and conservative surgery in cervical cancer have been published, accounting for 69 cases. The use of NACT allowed fertility-sparing surgery in 56 women (81%). Squamous tumors were 32 (57%) and adenocarcinomas 24 (43%). Patients with tumor size >2 cm were 34 (64%). Most Authors used TIP or TEP regimens.

Results: Complete or optimal pathologic response after NACT was observed in 46 cases (82%). Only three invasive relapses (all in the same series) have been observed in the ovary (1 case, dead of disease) and in the cervix (two cases, currently alive) and underwent demolitive surgery. Furthermore three patients (all from another series) presented with low- or high-grade cervical dysplasia during the follow-up and were managed conservatively.

Twenty-six women (46%) attempted to conceive: 31 healthy babies were born (two before 32 weeks) while 3 miscarriages (one during second trimester) were recorded.

Conclusions: Pregnancy outcomes after NACT and fertility sparing surgery are satisfactory, and the recurrence rate of 5% is acceptable. Women who would previously lose the option for future childbearing in exchange for cure are now seeing similar survival rates and successful pregnancy chances. In carefully selected patients with tumors larger than 2 cm who respond to NACT oncological outcomes can be preserved. Permanent damage to fertility from the use of chemotherapeutic agents has not been demonstrated in these series.
Meet the Professor HOW TO MANAGE THE LATE EFFECTS OF TREATMENT

SESSION INTRODUCTION / LATE EFFECTS OF TREATMENT FOR GYNAECOLOGICAL CANCER; PELVIC RADIOTHERAPY

R.A. Nout
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Treatment of gynaecological cancer covers a broad range of tumor types and treatments. Long-term or late effects include changes in sexual functioning, infertility, symptoms associated with early onset of menopause, anxiety, fatigue, bowel and urinary symptoms with increased frequency, urgency and/or incontinence, lymph edema and susceptibility to recurrent erysipelas. Over the past decades, improvements in the treatment of gynaecological cancers and increasing life expectancy have led to an increasing number of long-term cancer survivors, which stresses the importance of prevention and management of long-term effects.

Implementation of minimally invasive surgery, sentinel node biopsy, intensity modulated radiotherapy, image-guided brachytherapy and risk based selection algorithms for adjuvant treatment have led to a considerable decrease in treatment-related side effects. However, combined modality treatment (surgery, radiotherapy, and/or chemotherapy) and dose intensification are associated with an increased risk of side effects. It should also be kept in mind that the current long-term survivors have received their treatment in the years before the implementation of such modern techniques. Health-related quality of life studies in long-term cancer survivors indicate that the late effects of treatment can have an ongoing and persisting effect on patient functioning and long-lasting symptoms several years after treatment.

The purpose of this introduction is to provide an overview of late treatment effects; their impact on patient-reported quality of life, and strategies to counteract these late effects, and by doing so create awareness amongst health providers of the importance of these issues. The following presentations in this session will focus on survivorship care plans as a means to provide structural care for long-term cancer survivors in clinical practice, and on the recently developed international guidelines for vaginal dilation and assessment of psychosexual needs.
Meet the Professor HPV VACCINATION, MAKING A DIFFERENCE IN GLOBAL CANCER INCIDENCE RATES

HPV VACCINATION, MAKING A DIFFERENCE IN GLOBAL CANCER INCIDENCE RATES - AFRICA AND EU

L.A. Denny

Obs and Gynae, University of Cape Town, Cape Town, South Africa

The availability of two commercially available vaccines that prevent infection with the two most common HPV types associated with cervical cancer (HPV types 16 and 19) and the second also against types 6 and 11 (causative agent of low grade intraepithelial neoplasia and genital warts) has altered the landscape for the prevention of cervical cancer. While secondary prevention of cervical cancer with mass, cytology-based organised programs significantly reduced the incidence of and mortality from cervical cancer in the last century (in those countries that implemented the programs effectively), no developing countries have managed to initiate or sustain effective screening programs. This has resulted in 86% of the newly diagnosed cases of cervical cancer being found in the developing world, with a very high mortality rate due to late presentation and the lack of availability of appropriate diagnostics and treatment. HPV vaccination is likely to have a major impact on reducing cervical cancer in Africa and Europe - the challenge though is implementation of the vaccine. The vaccine should ideally be administered to girls (and if resources allow) boys prior to the onset of sexual activity due to the prophylactic nature of the vaccine. In most African and other developing countries there are relatively strong vaccine programs for children up to age 6 but thereafter the coverage reduces significantly. HPV vaccination will require the creation of a new platform for the delivery of the vaccine, and most studies to date suggest that these should be school-based and according to grade, rather than age. In countries with many other health needs it will be important to link HPV vaccination to other important health interventions e.g. Vit A supplementation, booster doses of tetanus, diphtheria, nutritional assessment and others according to regional priorities.
Meet the Professor HPV VACCINATION, MAKING A DIFFERENCE IN GLOBAL CANCER INCIDENCE RATES

HPV VACCINATION, MAKING A DIFFERENCE IN GLOBAL CANCER INCIDENCE RATES

B.J. Monk

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Cervical cancer accounts for more gynecology related deaths worldwide than any other malady thus making it the most important preventable disease in woman's health today. Although likely an underestimate, Parkin and colleagues reported that cervical cancer affected 493,243 women worldwide in 2002 thereby making it the second most common female cancer and the third most common cause of female cancer mortality with 273,505 deaths reported.

Cervical cancer is preventable and generally curable if detected early. Important strategies to reduce the risk of cervical cancer include screening through the use of the Papanicolau (Pap) test, human papillomavirus (HPV) testing and prophylactic HPV vaccination. Researchers have identified HPV, which is transmitted through sexual contact, as the main cause of cervical cancer. Although the exact financial burden of HPV is unknown, it is estimated that the annual direct medical costs associated with cervical cancer treatment in the US range between 300 and 400 million US dollars and that the annual direct medical costs associated with cervical intraepithelial neoplasia (CIN) in the US range between 700 million and 2.3 billion US dollars. Clearly, widespread HPV vaccination is the most promising approach to reducing the cost, morbidity and mortality related to cervical cancer. Using non-infectious virus-like particles, HPV vaccination has been shown to be virtually 100% effective in preventing persistent type-specific HPV infections as well as their neoplastic sequelae. Fortunately, idiosyncratic toxicities have not been reported with HPV vaccination, although the durability of the vaccine induced immunity is unknown.

Since the approval by the Food and Drug Administration (FDA) of the quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine [Gardasil®, Merck and Co., Inc., Whitehouse Station, New Jersey, USA] on June 8th, 2006, the world has seen a rapid endorsement of widespread HPV vaccination. On June 29th, 2006, the Center for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) recommended routine vaccination of females 11-12 years of age with three doses of the quadrivalent HPV vaccine. The ACIP also recommended “catch up” HPV vaccination to young girls and adolescents between the ages of 9 and 26 in parallel with the approved FDA labeled indication. Although the vaccine is ideally administered before potential exposure to HPV through sexual contact, the ACIP recommended that the HPV vaccination “should be administered to females who might have been exposed to HPV including those already sexually active”. Barriers to widespread vaccination have been identified such as poor reimbursement for HPV immunization, challenges to vaccine distribution, the availability of HPV vaccination to underserved populations, and the misconception that HPV vaccination will increase sexual activity and promote promiscuity.

As more and more people are vaccinated, the need and cost effectiveness of cervical cancer screening will decrease. How many individuals need to be vaccinated and how protective does the HPV vaccination need to be before screening recommendations change? Will Pap testing still be necessary with widespread vaccination or will HPV testing be the preferred test in the future? Clearly, saving money through altered cervical cancer screening paradigms such as extended intervals for Pap testing may help make HPV vaccination cost effective in developed countries where the risk of cervical cancer is proportionally low compared to underdeveloped countries.

HPV vaccination is not about the virus. It is about patients, one by one, who need to be protected against the harmful effects of HPV infection. We cannot forget the perspectives of the patients that we see daily. Finally, the future holds new indications for HPV vaccination, the inclusion of more HPV types into vaccines and new strategies such as unique adjuvants to enhance vaccine effectiveness.
Although the future for HPV vaccination is bright, we cannot delay the adaptation of widespread HPV vaccination until newer or better HPV vaccines emerge.

References:


Meet the Professor OBESITY AND GYNECOLOGIC ONCOLOGY: A GROWING EPIDEMIC

OBESITY AND GYNECOLOGIC ONCOLOGY: A GROWING EPIDEMIC

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Obesity is becoming an epidemic in many parts of the world and is expected to supersede malnutrition as the biggest nutritional threat within our lifetime. While the mechanisms by which obesity induces or promotes tumorigenesis are varied, obesity is associated with an increased risk of several malignancies, including endometrial and ovarian cancer. Data regarding the role that BMI may play with clinical outcomes are conflicting with studies showing worse and similar outcomes for obese women with endometrial cancer. However, higher BMI is associated with lower quality of life in these women and as physicians we should attempt to improve the quality of life of our patients whenever possible. This has lead to the interest in minimally invasive surgery for our patients with gynecologic malignancies. Obesity poses challenges for gynecologic oncologist as related to the surgeries that are a hallmark of our multi-modality approach to cancer care. This course will review the issue of obesity in gynecologic oncology with a focus on the surgical implications including route of surgery and anesthetic issues.

Objectives:

1) To appreciate the increasing problem that obesity presents to gynecologic oncology patients with regards to the incidence and outcomes related to their malignancies.

2) To better understand the anesthetic concerns in those patients undergoing surgery for their malignancies in an effort in improve collaborations with your anesthesia colleagues.

3) To better understand the opportunities and challenges associated with MIS in women with obesity and gynecologic malignancies.
Meet the Professor PALLIATIVE CARE AND SEXUALITY IN WOMEN WITH ADVANCED GYNECOLOGICAL CANCER

PAIN MANAGEMENT IN WOMEN WITH CANCER IN DEVELOPING COUNTRIES

L.A. Denny

Obs and Gynae, University of Cape Town, Cape Town, South Africa

Cancer is considered a relatively rare disease in Africa, largely due to the overwhelming prevalence of competing diseases such as Malaria, Tuberculosis, Human Immunodeficiency virus infections and maternal mortality among others. Yet it is estimated that there were over 650 000 cases of cancer diagnosed in Africa in 2008, and over 80% of these patients died from their disease. The commonest gynaecological cancer in African women is cervical cancer (approximately 80 000 new cases per year and just over 50 000 deaths) and the majority of women present with advanced and untreated disease. Palliative care exists in isolated pockets in the African content and only 22 countries have any access to anti-cancer therapies such as radiation and chemotherapy. surgical oncology is also rarely available, even in a palliative setting, for instance for colostomy to divert rectovaginal fistulae. Where these therapies do exist they are hopefully inadequate; for instance there is one radiation machine for 60 million Ethiopians. Further, only 11 countries in Africa allow the use of oral morphine, due to fears of illegal use or abuse. Thus management of pain in women with advanced gynaecological malignancies is usually extremely poor, leaving women to die painful, undignified deaths, often isolated and alone. Developing a plan for the palliation of women with gynaecological cancer will require the synergy of many roleplayers, from politicians to health care professionals to patient advocacy groups.
Meet the Professor PALLIATIVE CARE AND SEXUALITY IN WOMEN WITH ADVANCED GYNECOLOGICAL CANCER

PALLIATIVE CARE AND SEXUALITY IN WOMEN WITH ADVANCED GYNECOLOGICAL CANCER

M. Quinn

University of Melbourne, Melbourne, VIC, Australia

It is still extraordinary that the so much effort is placed on the multimodality approach to cancer care, yet those factors which impact so profoundly on the end of life (EOL) are so under-researched and thereby so poorly understood. It is inevitable that the resources available for ensuring an individualised approach to EOL issues will vary enormously. Variation, however, in physician approach should be able to be minimised by recognising the value of continued care giver-patient interaction, the need for ongoing empathy and the emphasis on simple measures to ensure pain control. This presentation will concentrate on those factors which we can influence early in the disease trajectory and how we can best ensure quality EOL. Particular emphasis on palliative care in resource constrained areas will be made.
Meet the Professor PALLIATIVE CARE AND SEXUALITY IN WOMEN WITH ADVANCED GYNECOLOGICAL CANCER

S. Carr
Psychosexual Medicine, Royal Womens Hospital, Melbourne, VIC, Australia

Sexuality is inherent in everyone, and the expression of one's gender identity, sexual orientation and sexual feelings and behaviour can alter over a lifespan, depending on life circumstances. Cancer and its treatments can have a major impact on sexuality, again fluctuating as the cancer progresses affecting not only the individual, but their partner if they have one. Despite the knowledge that at least half of women with cancer will have sexual difficulties at some stage, there is still consistent evidence that sexual issues are not always routinely discussed in the clinical setting, despite the patients wishing to do so.

Sex in the palliative phase is even more sensitive, and consequently is under researched.

The presentation will discuss some of the problems faced in this area by both patients and clinicians, and discuss possible alternative strategies for improvement.
Meet the Professor RADIATION RECALLED: A 'NEW" MODALITY FOR OVARIAN CANCER

RADIOTherapy in Ovarian Cancer: WHEN IF EVER?

G. Thomas

Radiation Oncology, Sunnybrook Odette Cancer Centre, Toronto, ON, Canada

Radiation therapy in the adjuvant or curative setting for ovarian cancer has largely been abandoned. The identification of active systemic agents such as Platinols and Taxanes amongst others, created a pressure to avoid wide field abdominal pelvic irradiation because of possible compromise to bone marrow tolerance and fear of serious GI complications. However, strong evidence exists for the radiation sensitivity of ovarian cancers. In the 1980's whole abdominal radiation without the use of any chemotherapy was shown to be curative as post surgical adjuvant treatment in a substantial proportion of patients with microscopic or small volume residual disease. In addition, numerous articles have been published attesting to the persistent radio sensitivity of ovarian cancers in the palliative setting despite failure of multiple lines of chemotherapy. Recent retrospective evidence suggests that radiation may be of incremental adjuvant benefit when added to chemotherapy particularly for non serous types of ovarian cancer. Evidence for this efficacy of radiation will be presented. In addition, the current role of radiation in palliation or treatment of pelvic confined or nodal confined recurrences after chemotherapy will be discussed.

Future treatments for ovarian cancer will undoubtedly differ according to the molecular and genetic characteristics of different histologic sub-types. It may include the use of radiation particularly when molecular profiling is done to elucidate factors contributing to radiation sensitivity/resistance. Where wide field abdominal radiation may be indicated newer techniques of radiation delivery may substantially spare organs at risk and allow for an integrated role with systemic therapies and other radiation sensitizers.
Meet the Professor SENTINEL NODE MAPPING IN GYNECOLOGIC CANCERS

WHAT TYPE OF TRIALS DO WE NEED FOR SENTINEL NODE SURGERY IN GYNAECOLOGIC ONCOLOGY?

H. Kitchener

Academic Unit of Obstetrics and Gynaecology, The University of Manchester, Manchester, UK

Sentinel node surgery as an indicator of lymphatic metastasis is not only feasible in gynaecologic oncology, but has to some extent been proven in principle. Its clinical value relies on a high negative predictive value, sensitivity to detect nodal metastases and the potential to reduce surgical mortality and long term treatment effects such as lymphoedema.

In order to determine its role in terms of achieving standard of care, a solid evidence base is essential, which in turn would require to demonstrate true clinical effectiveness and cost effectiveness.

This process is most advanced in vulval cancer with the GROINS trials, but potential value has also been shown for endometrial and cervical cancer. Some of the questions that arise include the following:

Is radioactive colloid always required to achieve optimal sensitivity or is blue dye sufficient?

Does sentinel node surgery provide adequate sensitivity in the detection of metastatic nodes?

Do immunohistochemical epithelial markers indicate true malignant metastases?

Can sentinel node status direct adjuvant therapy as effectively as systemic node dissection?

Is sentinel node surgery associated with equivalent survival rates combined with reduced morbidity and reduced longer term effects?

The clinical trials which are required to address these different questions will differ in design. Some would require randomisation, others require only dual procedures and follow-up. Some endpoints are almost immediate and others long term. These include determination of node status, morbidity, survival, quality of life and cost effectiveness over a time horizon extending to overall survival. There are issues such as the incidence of disease, demonstration of non inferiority as apposed to superiority, learning curves and patient acceptability, all of which impact on the feasibility of trials. These issues and the implications for trials going forward will be presented.
Meet the Professor WHAT IS INTEGRATIVE ONCOLOGY AND CAN IT HELP MY PATIENTS?

ACUPUNCTURE FOR CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

A. Goodman
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Background: Powerful anti-emetics have controlled disabling chemotherapy induced nausea and vomiting for many patients. However, significant side effects continue to impair patients' quality of life. Alternate modalities such as acupuncture have been used to alleviate the effects of chemotherapy.

Objective: The experience of patients who received acupuncture in the Cancer Center at Massachusetts General Hospital is reviewed and the world's literature on this topic is analyzed.

Patients: The medical records of patients undergoing acupuncture during chemotherapy from 2003 to 2009 were reviewed. A patient self-reporting scoring system used 0 = no change, 1= mild improvement (< than 50% response), 2= moderate improvement (> 50% response), 3 = complete resolution.

Results: From 2003 to 2009, there were 899 patient encounters for acupuncture. All patients on chemotherapy received ondansetron. Using the patient self reporting scoring system, complete resolution of systems was as follows: anxiety 90%, constipation 100%, neuropathy 50%, nausea 70%, vomiting 80%, joint pain 40%. Acupuncture points Pericardium (PC) 6 and Spleen (SP) 9 were most commonly used.

Conclusion: This retrospective review of the effect of acupuncture on nausea, vomiting, and other symptoms during chemotherapy at Massachusetts General Hospital suggests a robust alleviation of multiple symptoms. Many studies have also concluded that acupuncture may alleviate chemotherapy-induced nausea and vomiting and may be useful for symptoms that are refractory to standard premedication.
Opening Plenary Session on Ovarian Cancer

INCREASED RISK FOR OVARIAN CANCER AND BORDERLINE OVARIAN TUMOURS IN SUBFERTILE WOMEN WITH ENDOMETRIOSIS

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Background: There is increasing evidence of an association between endometriosis and increased risk of ovarian cancer. However, most reports were based on self-reported diagnosis of endometriosis. In a large cohort of subfertile women we investigated whether ovarian or extra-ovarian endometriosis was associated with increased risk of ovarian cancer and borderline ovarian tumours (BOT).

Methods: We conducted a nationwide historic cohort study among women with subfertility problems between 1980-1995. For this analysis we selected all cohort members with (n=3,657) and without (n=5,247) evidence of endometriosis. 78% of diagnoses of endometriosis were confirmed by surgery and/or pathology reports. We linked the cohort with the Dutch Pathology Database and the Netherlands Cancer Registry to assess the occurrence of ovarian cancer and BOT.

Results: We observed a strongly increased risk of all ovarian malignancies combined in women with endometriosis (hazard ratio (HR) 8.2; 95% CI 3.1 - 21.6). The HR associated with endometriosis was 12.4 (95% CI 2.8 - 54.2) for ovarian cancer and 5.5 (95% CI 1.5 - 20.2) for BOT. Both ovarian and extra-ovarian endometriosis (HRs 11.3, 95% CI 4.0 - 31.8 and 7.7, 95% CI 2.1 - 28.7, respectively) carried a significantly increased risk for ovarian cancer and BOT.

Conclusions: Endometriosis is a strong risk factor for ovarian cancer and BOT in subfertile women.
Opening Plenary Session on Ovarian Cancer

SPECIALIZED PATHOLOGY REVIEW IN PATIENTS WITH OVARIAN CANCER: HIGHLY RECOMMENDED TO ASSURE ADEQUATE TREATMENT. RESULTS FROM A PROSPECTIVE STUDY

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Background: In view of retrospective findings on second opinion pathology in ovarian cancer, it seems certain that a considerable number of ovarian borderline tumors (BOTs) or metastatic non-ovarian primaries are being erroneously diagnosed as ovarian carcinomas. If BOTs are misdiagnosed as cancer, patients may not only suffer from non-beneficial morbidity but may have to cope with an incorrect diagnosis of cancer for the rest of their lives. We hypothesized that 5% of German ICON7 patients have lesions in conflict with inclusion criteria.

Design: Patients who were enrolled into the ICON7 trial in Germany were asked to consent to a translational subprotocol. Contributing pathologists were asked to submit all original slides. Specialized central pathology review was performed by two experienced gynecopathologists. If a given discrepancy could not be resolved by discussion with the local pathologist, a panel of experts was available for clarification.

Results: 454 patients diagnosed with ovarian carcinoma were recruited. In 6.8% a major discrepancy of potential clinical relevance was found. Divergent histological typing was found in 28.2%.

Conclusion: This study clearly shows that central pathology review by experienced gynecopathologists is highly recommendable if overtreatment with chemotherapy of patients with BOTs and inadequate treatment of patients with ovarian metastases is to be avoided in the future. In order to further optimize the quality of care, a high throughput infrastructure for specialized pathology review will have to be established. The authors propose a new internet-based ovarian cancer network, capable of providing specialized second opinion pathology within 10 working days.
Opening Plenary Session on Ovarian Cancer

COPY NUMBER CHANGES OF 4-GENE SET PREDICT EARLY RELAPSE IN EPITHELIAL OVARIAN CANCER AFTER INITIAL PLATINUM-PACLITAXEL CHEMOTHERAPY

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Objective: To determine the genes that potentially distinguish patients with short versus long time to recurrence(TTR) after initial platinum-paclitaxel(PP) chemotherapy in advanced epithelial ovarian cancer(EOC).

Methods: Tumor samples of 160 advanced EOCs were obtained during the primary cytoreduction. Array comparative genomic hybridization(aCGH) was carried with genomic DNA from 17 EOCs(8 with TTR>15 months, 9 with TTR≤6 months) to screen candidate genes, copy-number changes(CNC) of which were significantly different between early and late relapse. In a 40-case training set and a 103-case validation set, CNC of candidate genes was evaluated by real-time PCR. Discriminant analysis was used to evaluate the accuracy of CNC of candidate genes in determining early or late relapse(TTR≤or>10 months) after initial PP in training and validation test.

Results: Seventeen candidate genes were identified by aCGH. CNC of candidate genes correctly distinguished 7 late and 9 early relapse tumors among the 17 EOCs by hierarchical clustering. Real-time PCR was utilized to analyze the CNC of the above 17 genes. Correlated analysis was done between the results of real-time PCR and aCGH. CNC of GSTT1, ISG20L1, STARD5 and FREM1 by real-time PCR were individually correlated with TTR(P< 0.05). 75.5% of a 40-case training set was correctly divided into early and late relapse by 4-gene CNC. In an independent 103-case validation set, the accuracy of 4-gene CNC in determining early or late relapse was 61.8%.

Conclusions: Four-gene CNC could determine early or late relapse(TTR≤or>10 months) after initial PP chemotherapy in advanced EOC. The proposed 4-gene set needs further validation.
Opening Plenary Session on Ovarian Cancer

INTRATUMORAL HETEROGENEITY IN HIGH-GRADE SEROUS CANCERS: DEFINING EVOLUTION OF THE SOMATIC MUTATIONAL LANDSCAPE ACROSS SPATIALLY AND TEMPORALLY SELECTED SAMPLES

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Treatment failure is often blamed on intratumoral heterogeneity (ITH). We wished to compare the genetic composition of high-grade serous (HGS) cancers separated spatially and temporally.

Patients undergoing primary debulking surgery (PDS) for HGS cancer were approached and our tumor bank searched for matched primary and recurrent HGS samples with normal controls. Chromosomal architecture, mutational profiling and deep targeted sequencing was undertaken by Affymetrix SNP6.0, exome capture, and PCRamplicon sequencing in Illumina or IonTorrent.

Five cases with 4-8 samples each (PDS) and one with primary & recurrent disease have been analyzed. Two PDS samples were from fallopian tube precursor lesions. We observed widespread variation between mutational profiles within patients however genomic architecture was more conserved. Regional samples showed non-overlapping clonally dominant mutations suggesting distinct evolutionary histories of synchronous anatomically distant sites of extraction. Anatomic sites of extraction and corresponding genetic landscape for the same case (Figure 1&2) and a case of primary (pre-neoadjuvant-treatment) and recurrent sample (post-treatment) (Figure3) are shown. Proximity of samples assessed spatially/synchronous was not associated with degree of similarity/differences between samples.

Intratumoral heterogeneity in HGS cancer may explain the discordant results observed with targeted therapies, and lack of success even when treatment is directed by biopsies (single) from the same patient. In depth genomic interrogation may enable us to understand the evolution from purported precursor lesions, and predict changes induced by selection pressures e.g., chemotherapy.
**Figure 1.** Synchronous samples obtained at primary debulking surgery from a. L fallopian tube, b-d. L ovary, e. L iliac node, f. R paracolic node, g. R ovary.
Figure 2. DG1009 five samples from debulking surgery copy number profile

[Figure 2]
Figure 3. DAH209/DAH890 primary/recurrence copy number profile

[Figure 3]
Opening Plenary Session on Ovarian Cancer

INCREASED TUBULIN-β-III EXPRESSION IN SEROUS CANCERS FOLLOWING PACLITAXEL ADMINISTRATION: IMPLICATIONS FOR MECHANISMS OF RECURRENT DISEASE

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Introduction: Though chemotherapy kills the majority of tumor bulk, chemoresistant cancer stem cells may remain and contribute to tumor propagation and recurrence. Tubulin-β-III may confer paclitaxel resistance, and overexpression may signify dedifferentiation concurrent with acquisition of progenitor properties.

Objectives: To characterize tubulin-β-III expression in (1)fresh-frozen tissues representing chemotherapy-naïve/chemotherapy-treated patients (2)cell lines following in vitro paclitaxel exposure (3)CD44-enriched and CD44-deficient cell lines in relationship to paclitaxel chemoresistance.

Methods: Tubulin-β-III was quantified by RT-PCR in unmatched specimens (37-chemotherapy-naïve/14-chemotherapy-treated stage III/IV serous ovarian cancers) then correlated with immunohistochemistry (IHC)(n=13) and overall survival (OS). Changes in tubulin-β-III in 10 established uterine and ovarian serous cell lines were determined after subculture in escalating doses of paclitaxel across 18 weeks. IC₅₀,paclitaxel was compared between CD44-enriched and CD44-deficient cell populations.

Results: Tables 1/2 illustrate source specimen/cell line characteristics. Chemotherapy-naïve specimens obtained via primary debulking expressed less tubulin-β-III relative to non-naïve counterparts obtained at interval debulking; tubulin-β-III expression correlated with OS (Figures-1a/b). Subculture in paclitaxel caused upregulation of tubulin-β-III (Figure-1c). IHC reflected copy number; mean score among primary versus interval debulking specimens was 0-1+ versus 2-3+(p=0.036). Compared to CD44+ cell lines, CD44+ populations expressed more tubulin-β-III and preliminarily showed greater resistance to paclitaxel (Figure-2a/b).

Conclusions: Upregulation of tubulin-β-III is one plausible mechanism for development of chemoresistant recurrent disease. Paclitaxel administration may select for populations capable of tubulin-β-III overexpression.
<table>
<thead>
<tr>
<th>STAGE</th>
<th>PRIMARY DEBULking (n=37)</th>
<th>%</th>
<th>INTERVAL DEBULking (n=15)*</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
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<tr>
<td>II</td>
<td>0</td>
<td>0.0</td>
<td>1</td>
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</tr>
<tr>
<td>III</td>
<td>26</td>
<td>70.3</td>
<td>11</td>
<td>71.3</td>
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<tr>
<td>IV</td>
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<td>2</td>
<td>5.4</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**A6E, mean [range] (y)**: 57.6 [24-77] 60.4 [37-77]

* Twelve patients received neoadjuvant chemotherapy, 3 patients presented with recurrent disease.

Table 1: Source patient characteristics for fresh-frozen tissue samples.

<table>
<thead>
<tr>
<th>CELL LINE</th>
<th>MAXIMUM PACLITAXEL EXPOSURE [nM]</th>
</tr>
</thead>
<tbody>
<tr>
<td>O3PC-1</td>
<td>150</td>
</tr>
<tr>
<td>O3PC-3</td>
<td>50</td>
</tr>
<tr>
<td>O3PC-4</td>
<td>120</td>
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<tr>
<td>USPC-AIK-1</td>
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<tr>
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<td>600</td>
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<tr>
<td>USPC-AIK-5</td>
<td>20</td>
</tr>
<tr>
<td>USPC-AIK-9</td>
<td>800</td>
</tr>
<tr>
<td>USPC-AIK-15</td>
<td>600</td>
</tr>
</tbody>
</table>

Table 2: Paclitaxel dosing for ovarian (O3PC) and uterine (USPC) serous papillary cell lines.

[Tables 1 and 2]
Figure 1: [a] Tubulin-β-III is overexpressed in chemotherapy-treated relative to chemotherapy-naïve disease. Copy number by RT-PCR is shown for fresh-frozen specimens. [b] Among patients who underwent primary debulking with adequate follow-up, low tubulin-β-III expression predicted improved overall survival. [c] Subculture with increasing doses of paclitaxel for approximately 18 weeks (i.e., the equivalent of 6 cycles) induces upregulation of tubulin-β-III in established serous cell lines.
Figure 2: [a] Cell lines that express the stem cell marker CD44 demonstrate overexpression of tubulin-β-III relative to CD44-negative populations and are more resistant to paclitaxel. A representative dose-response curve is shown [b].
Opening Plenary Session on Ovarian Cancer

PROSPECTIVE STUDY OF BORDERLINE-TUMORS OF THE OVARY: ROLE OF PROGNOSTIC MARKER AND CLINICAL-OUTCOME. A PROJECT OF AGO STUDY GROUP


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Background: Borderline ovarian tumors (BOT) are a rare tumor entity and limited data exist based on retrospective analysis. Therefore we performed a prospective study including a central pathology review.

Methods: All consecutive patients diagnosed with BOT 1998-2008 in 24 German institutions were enrolled. Tumor samples were sent for central histopathological review to experienced pathologists. All clinical outcome parameters were updated.

Results: Pathological review was performed in1,058 of 1,237 pts resulting in 950 confirmed BOT cases. Under- and overdiagnosis was observed in 5.0% and 6.2% of all cases. Median age was 49 years; 85% of patients were diagnosed in FIGO stage I. Serous type (S-BOT) was diagnosed in 68% and the mucinous type (M-BOT) in 31%. Primary/re-staging surgery led to complete resection in 92% of pts (residual disease 1.3%, unknown 6.4%). Adjuvant chemotherapy was given to 33 (3.5%) pts only. 166 (17%) underwent fertility preserving surgery and 31 (19%) of these patients had documented pregnancies thereafter. Overall, 74 (7.8%) pts suffered from relapse and 43 (4.57%) died, transformation to invasive cancer was observed in 30% of the relapses. Inadequate surgical staging, residual tumor, fertility sparing surgery and higher FIGO stage were associated with reduced progression-free survival.

Conclusions: To this day, this is the largest data set available for BOT. Prognosis of BOT is generally excellent without any adjuvant therapy. Adequate staging is very important and influence the clinical outcome.
Opening Plenary Session on Ovarian Cancer

BDCA-3+ AND CD16+ DENDRITIC CELLS AND CD8+ T CELLS IN ADVANCED EPITHELIAL OVARIAN CANCER ASSOCIATED ASCITES PREDICT DISEASE COURSE

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1Radboud University Nijmegen Medical Centre, 2Tumorimmunology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Despite optimal treatment, 80% of patients with epithelial ovarian cancer will develop recurrence of disease. The influx of diverse immune cells in the tumor suggest a pivotal role in controlling the growth of the malignant tumor. However, this influx is partially balanced by ovarian cancer cells that exploit several ways to counteract immune cell reactivity. We measured the presence of the different subsets of dendritic cells and T cells in ovarian cancer associated ascites of 42 woman by flow cytometry. Dendritic cells were divided in myeloid DCs (mDCs; BDCA-1+, BDCA-3+, CD16+ DCs) and plasmacytoid DCs. We show that all DC subsets are present in ovarian cancer associated ascites. Normalization of CA125 after neo-adjuvant chemotherapy was correlated to high BDCA-3+ mDCs. BDCA-1+ mDCs are not predictive markers of surgical outcome, CA125 normalization or survival. High CD16+ mDCs were strong correlated with overall survival and disease free survival. High CD8+ T cells and low CD4+ T cells were correlated with normalized CA125 levels after completed treatment but not after neo-adjuvant chemotherapy. Low CD4/CD8 ratios were correlated to normalization of CA125 levels after completed treatment and disease free survival. Our results implicate cooperation between BDCA-3+ mDCs and CD8+ T cells in patients who are treated with neo-adjuvant chemotherapy. CD16+ mDCs produce high levels of interleukin-12 and induce naïve T cell differentiation into T helper-1 cells and this seems to be highly important in survival rates. These results underline the importance of DC and T cell involvement in patients with ovarian cancer.
Opening Plenary Session on Ovarian Cancer

THE EFFICACY OF A REGIONAL NETWORK FOR OVARIAN CANCER CARE: A POPULATION-BASED STUDY


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Background: To optimize treatment of epithelial ovarian cancer (EOC) patients a regional collaboration was introduced in the eastern part of the Netherlands in 2000. Gynecologic oncologists from the university center are invited to conduct surgery in the satellite community hospitals if EOC is considered based on the Risk of Malignancy Index (RMI) and/or clinical suspicion. We studied the changes in surgery and survival with the start of this collaboration.

Methods: The data of all 1554 EOC patients diagnosed between 1996 and 2010 in eleven hospitals were collected. The surgical results were studied in three calendar periods (1996-1999, 2000-2004 and 2005-2009) and compared using t-tests and χ²-tests. Kaplan-Meier survival curves of progression-free survival and overall survival before (1996-2000) and after the collaboration (2001-2005) were compared using log-rank tests.

Results: Adequate staging was performed in 36.7% of the patients before versus 66.9% after the start of the collaboration (p<0.01). In case of RMI >200, staging was more often performed by a gynecologic oncologist (87.7% versus 33.9%, p<0.01). In advanced stage patients (FIGO ≥IIb) both an optimal result after debulking (i.e. residual volume < 1 cm) and a complete debulking (no residual disease) were achieved more often after the start of the collaboration, 57.4% versus 76.5% (p<0.01) and 24.1% versus 43.4% (p<0.01). During the study period there was a trend towards improved survival.

Conclusions: Gynecologic oncologists attended more surgeries since the start of the collaboration resulting in better surgical outcome and a trend towards increased survival. The regional collaboration has led to improvement of care for EOC patients.
Opening Plenary Session on Ovarian Cancer

CLINICAL OUTCOME OF BRCA1- COMPARED WITH BRCA2-ASSOCIATED EPITHELIAL OVARIAN CANCER: A NATIONWIDE STUDY IN THE NETHERLANDS

P. Vencken\(^1\), W. Reitsma\(^2\), M. Mourits\(^3\), G. de Bock\(^3\), J. de Hullu\(^4\), A. van Altena\(^5\), K. Gaarenstroom\(^6\), H. Vasen\(^6\), M. Adank\(^7\), H. Trum\(^7\), H. Meijsers-Heijsber\(^7\), M. Schmidt\(^8\), K. Jeanson\(^8\), R. Zweemer\(^9\), G. Fons\(^10\), B. Slangen\(^11\), C. Burger\(^1\), M. Kriege\(^12\), C. Seynaeve\(^12\)

\(^1\)Department of Obstetrics and Gynecology, Division of Gynecological Oncology, Erasmus MC University Medical Center, Rotterdam, \(^2\)Department of Obstetrics and Gynecology, Division of Gynecological Oncology, \(^3\)Department of Obstetrics and Gynecology, Division of Gynecological Oncology, University Medical Center St Radboud, Nijmegen, \(^4\)Department of Obstetrics and Gynecology, Division of Gynecological Oncology, Leiden University Medical Center, \(^5\)Medical Director of the Netherlands Foundation for the Detection of Hereditary Tumours, Leiden, \(^6\)Department of Clinical Genetics, VU University Amsterdam, \(^7\)Department of Obstetrics and Gynecology, Division of Gynecological Oncology, University Medical Center Utrecht, Utrecht, \(^8\)Department of Obstetrics and Gynecology, Division of Gynecological Oncology, Amsterdam Medical Center, \(^9\)Department of Obstetrics and Gynecology, Division of Gynecological Oncology, University Medical Center-Daniel den Hoed Cancer Center, Rotterdam, The Netherlands

Background: Recent studies reported a longer overall survival (OS) for BRCA2- versus BRCA1-associated epithelial ovarian cancer (EOC), potentially due to a different chemosensitivity. However, chemosensitivity and progression-free survival (PFS) were not evaluated yet.

Aim: To explore chemosensitivity, PFS and OS of BRCA1-versus BRCA2-associated EOC in a nationwide cohort of Dutch patients.

Methods: A consecutive series of 245 BRCA1-and 99 BRCA2-associated EOC patients (diagnosed 1980-2010) were identified through the family cancer clinics of all Dutch university hospitals, the Netherlands Cancer Institute and the The Netherlands Foundation for the detection of Hereditary Tumours. Demographics, tumor-characteristics, treatment-characteristics and follow-up data were collected. Outcome measures were response to first-line chemotherapy, PFS and OS. Statistical analyses were performed using the chi-square test, Kaplan-Meier and Cox-regression methods.

Results: Age at diagnosis was younger in BRCA1 than BRCA2 patients (median 51 versus 55 years, \(P< 0.001\)), while mainly advanced stage was observed (FIGO III/IV: BRCA1 75%, BRCA2 71%, \(P=0.16\)). After primary therapy CR/No Evidence of Disease was observed in 86% of the BRCA1-versus 90% of the BRCA2 patients, while PD was observed in only 5 BRCA1 patients (\(P=0.36\)). PFS was 3.9 years in BRCA2 (95%-CI 2.5-5.3) versus 2.2 years in BRCA1 EOC patients (95%-CI 1.9-2.5; \(P=0.006\)). OS was 9.7 years in BRCA2 (95%-CI 5.0-14.3) versus 6.0 years in BRCA1 patients (95%-CI 5.1-6.9; \(P=0.04\)).

Conclusions: BRCA2-associated EOC patients have a significantly longer PFS and OS compared with BRCA1 patients after primary therapy, including chemotherapy. Differences could not be explained by age at diagnosis, FIGO stage or chemosensitivity.
Plenary Session on Cervical Cancer

HPV FOCAL: FIRST ROUND SCREEN RESULTS FROM A RANDOMIZED CONTROLLED TRIAL IN A CANADIAN POPULATION BASED PROGRAM

T. Ehlen1, G. Ogilvie2, D. van Niekerk3, M. Krajden4, R. Martin5, G. Stuart6, S. Peacock6, L. Smith7, E. Franco8, A. Coldman7

1Gynecologic Oncology, BC Cancer Agency/Vancouver General Hospital, 2STI Division, BC Centre for Disease Control, 3Cervical Cancer Screening Program, BC Cancer Agency, 4Hepatitis Division, BC Centre for Disease Control, 5Medicine, University of British Columbia, 6Health Economics, 7Population Oncology, BC Cancer Agency, Vancouver, BC, 8Epidemiology, McGill University, Montreal, QC, Canada

Objectives: HPV FOCAL is a population based trial comparing the efficacy of primary hr-HPV DNA testing (HPV positive undergo reflex cytology) to cytology (Liquid based, LBC) alone. Results of round 1 screening presented.

Methods: 25,000 British Columbia women aged 25 to 65 assigned to either: Control: LBC testing with reflex hr-HPV testing if ASCUS; Negatives screen again at 2 and 4 years. Colposcopy referral >LSIL or ASCUS/HPVpositive. HPV: hr-HPV testing with reflex cytology if HPV positive. Colposcopy referral HPVpositive/>ASCUS, rescreen in 12 months if HPVpositive/cytology negative. Exit screen at 2 or 4 years. Exit colposcopy referral at >ASC-US or HPV-positive.

Outcomes: Confirmed ≥CIN3 at 4 year exit screen in control and HPV arm.

Conclusions: Data available for 22,072 completed round 1. Overall colposcopy referral 40.2/1000 in control and 59.1/1000 in the HPV arm. To date, overall CIN2+ and CIN3+ rates are 10.6/1000 and 4.9/1000 in control and 16.2/1000 and 7.8/1000 in HPV arm. In the control arm, ASCUS/HPVnegative women with repeat cytology in 12 months, no cases of CIN2+ detected (PPV=0%). In comparison, those baseline HPVpositive /cytology negative in the HPV arm, still HPV positive12 months later, CIN2+ rate was 230.8/1000 (PPV=23.1%).

Preliminary results of round 1 screening show higher colposcopy referral rates in HPV arm. Comparing results for the follow-up screening round to date, the PPV in HPV arm was substantially higher than the control arm (0% vs 23.1%), indicating greater risk associated with persistent hr-HPV infection for precancerous lesions. Trial ongoing as women attend second round/exit screening.
Plenary Session on Cervical Cancer

A NEW SINGLE-PORT APPROACH TO PERFORM A TRANSPERITONEAL STEP AND AN EXTRAPERITONEAL PARA-AORTIC LYMPHADENECTOMY VIA A SINGLE INCISION

S. Gouy, C. Uzan, A. Leary, P. Morice
Institut Gustave Roussy, Villejuif, France

Aim: Report for the first time a new single port procedure to perform an extraperitoneal para-aortic lymphadenectomy for the staging of locally advanced cervical cancer before chemoradiotherapy.

Description of video presentation: This video presentation (duration: 7 minutes) shows the different surgical steps using only conventional instruments: description of the single 2-3 cm incision which was made perpendicular to a point situated 2/3 along the line drawn from the umbilicus to the anterior superior iliac spine; installation and insertion of the single port through this single incision to perform the transperitoneal step (to rule out peritoneal disease) and the para-aortic lymphadenectomy via an extraperitoneal approach; dissection of the different anatomical landmarks (psoas muscle, aortic bifurcation, ureters, inferior mesenteric artery, left renal vein, vena cava, azygos vein ...); dissection of nodal tissues from the aortic bifurcation to the left renal vein; extraction of nodal tissues via the single port. Figure 1 shows the appearance of the skin at the end of the procedure.

[Figure 1: Appearance of the skin at the end of the]
Conclusion: This video shows for the first time a new single port procedure to perform a transperitoneal step (to rule out peritoneal disease) and an extraperitoneal para-aortic lymphadenectomy via a single incision. This new single port procedure has been used routinely at our institution for the last months without conversion to laparotomy or conventional multiport laparoscopy.
Plenary Session on Cervical Cancer

ENHANCED PATIENT RECOVERY IN GYNECOLOGIC ONCOLOGY: A SEA CHANGE IN POST-OPERATIVE MANAGEMENT


Mayo Clinic, Rochester, MN, USA

Objective: To investigate whether our Enhanced Patient Recovery Protocol (ERP) (Table) results in earlier return of bowel function and reduced length of stay (LOS) with no change in post-operative morbidity.

Methods: Consecutive patients undergoing open debulking or staging surgery for gynecologic malignancy under ERP between 06/20/2011 and 12/20/2011 were prospectively identified. Historical controls were matched with cases by procedure. The Wilcoxon rank-sum and Chi-square tests were used for comparisons.

Results: No significant differences in patient characteristics were noted between the 166 cases and 166 controls. Surgery included bowel resection in 46%. IV narcotic use was reduced from 98.8% to 33% ($P< 0.0001$) with no change in pain scores 2 to 48 hours post-operatively. Rates of nausea/vomiting and NGT reinsertion were unchanged between groups, and cases showed earlier return of bowel function ($P< 0.0001$). ERP resulted in a median 4-day reduction in LOS ($P< 0.0001$) with stable readmission rate. No differences were observed in rate or severity of postoperative complications. Patient surveys showed that 95% rated satisfaction with post-operative care as excellent/very good.

Conclusions: Implementation of ERP in patients with gynecologic malignancies, including those undergoing extensive cytoreduction, resulted in earlier return of bowel function, reduced IV narcotic use and LOS, with stable readmission rate and post-operative morbidity. Traditional post-operative management including prolonged fasting, nasogastric suction, IV opioids, and excessive fluids serves no benefit to the patient.

<p>| Diet, Postoperative nausea and vomiting prophylaxis &amp; Activity | A) Diet: &lt;Preoperative&gt; • Evening before surgery: Carbohydrate loading drink • May ingest fluids up to 4 hours before procedure. &lt;Postoperative&gt; • No NGT; if NGT used intra-operatively, remove at end of procedure • General diet 4 hours after procedure • Day of surgery: 1 box of liquid nutritional supplement. Encourage oral intake of at least 800 mL of fluid, but no more than 2000 mL by midnight. • Day after surgery until discharge: 2 boxes of liquid nutritional supplement. Encourage daily oral intake of 1500-2500 mL of fluids. B) Postoperative nausea and vomiting prophylaxis: &lt;Intraoperative&gt; • Before incision (+/- 30 min): dexamethasone IV + droperidol IV • Before incision closure (+/- 30 min): granisetron IV. C) Activity: &lt;Postoperative&gt; • Evening of surgery: out of bed greater than 2 hours, including 1 or more walks and sitting in chair • Day after surgery and until discharge: out of bed greater than 8 hours including 4 or more walks and sitting in chair. • Patient up in chair for all meals. |
| Fluid balance | &lt;Intraoperative&gt; • Goal: maintain intraoperative fluid balance |</p>
<table>
<thead>
<tr>
<th><strong>Analgesia</strong></th>
<th>euvelema • Decrease crystalloid administration • Increase colloid administration; &lt;Postoperative&gt; • Operating room fluids discontinued upon arrival to floor • Fluids at 40 mL/hour until 08:00 am on day after surgery, then discontinued. • Peripheral lock IV when patient had 600 mL PO intake or at 08:00 am on day after surgery, whichever came first.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&lt;Intraoperative&gt;</strong></td>
<td>At induction: Celecoxib 400 mg + Gabapentin 600 mg • Opioids IV • After incision closure: injection of Bupivacaine at incision site; &lt;Postoperative&gt; • Goal: no patient controlled analgesia (PCA); oral analgesia • Oxycodone PO every 4 hours as needed for pain rated 4 or greater or greater than patient stated comfort goal • Scheduled acetaminophen every 6 hours • Scheduled NSAIDs: ketorolac IV every 6 hours for 4 doses, then ibuprofen PO every 6 hours • If patient unable to take NSAIDs: scheduled tramadol started at 06:00 am on day after surgery.</td>
</tr>
</tbody>
</table>

[Enhanced Patient Recovery Protocol]
Plenary Session on Cervical Cancer

PROSPECTIVE MULTICENTER STUDY EVALUATING THE SURVIVAL OF PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER (LACC) UNDERGOING LAPAROCOPIC PARA-AORTIC LYMPHADENECTOMY BEFORE CHEMORADIOThERAPY

S. Gouy1, P. Morice1, F. Narducci2, C. Uzan1, A. Rey1, A. Martinez3, P. Pautier1, D. Deandres1, D. Querleu3, C. Haie-Meder1, E. Leblanc1

1Institut Gustave Roussy, Villejuif, 2Centre Oscar Lambret, Lille, 3Centre Claudius Regaud, Toulouse, France

Aims: In 3 French Comprehensive Cancer Centers, patients with LACC were systematically staged using conventional and PET-CT imaging before chemoradiotherapy. If patients had no uptake in the para-aortic (PA) area, laparoscopic extraperitoneal staging surgery was then performed to define radiation field limits more accurately. The aim of this study was to evaluate the therapeutic impact of this management.

Methods: A prospective series including 237 patients treated from 2004 to 2011 for LACC with a negative PET-CT of the PA area and undergoing laparoscopic PA lymphadenectomy. Radiation fields were extended to PA area when PA nodes were involved. Chemoradiotherapy modalities were homogeneous between Institutions.

Results: Clinical stages were IB2 (n=79), IIA (n=10), IIB (n=120), III (n=23), IVA (n=5). The histologic types were squamous carcinoma (n=197), adenocarcinoma (n=34), adenosquamous carcinoma (n=3) and unknown (n=3). Twenty-nine (11%) patients had nodal involvement (false negative PET-CT results): 16 with PA nodal metastasis measuring > 5 mm and 13 ≤ 5 mm. With a median follow-up of 18 (range, 0-67) months, disease-free survival (DFS) at 2 years in patients without and with PA involvement was respectively 76% (68%-83%) and 61% (37%-80%)(p=.007). DFS at 2 years in patients without PA involvement or with PA metastasis measuring ≤or > 5 mm was respectively 76% (68%-83%), 89% (57%-98%) and 38% (14%-68%)(p=.0006).

Conclusion: This is the largest series of patients reported undergoing such strategy. We obtained the same survival rate for patients with PA nodal metastasis ≤5 mm and patients without PA lymph node involvement suggesting that this strategy is highly efficient in such patients. Conversely, the survival of patients with PA nodal involvement > 5 mm remained poor, despite no extrapelvic disease at PET-CT imaging in this subgroup. Other treatment modalities should be evaluated for these patients (adjuvant chemotherapy after extended field of chemoradiation therapy?).
Plenary Session on Cervical Cancer

TECHNIQUE OF NERVE-SPARING PARA-AORTIC LYMPHADENECTOMY (NSPAL) AND INTRA-/POSTOPERATIVE OUTCOMES IN STAGE IA-IIB CERVICAL CANCER

S. Mukhtarulina, I. Ushakov, A. Bobin, A. Popov, I. Aseeva

Gynecologic Oncology Department, Main Military Clinical Hospital named after N.N. Burdenko, Moscow, Russia

Objectives: To elaborate the technique of NSPAL; to determine the intra-/postoperative outcomes of NSPAL in patients with Ia-Iib stage cervical cancer.

Methods: 67 patients underwent radical hysterectomy type III or IV. 43 patients of the first group undergoing NSPAL (level 2 - n=1; level 3 - n=19; level 4 - n=23) were compared with 24 patients of the second group undergoing PAL (level 2 - n=10; level 3 - n=4; level 4 - n=10). Technique of NSPAL include the steps: 1) preserve superior hypogastric plexus and distal part of hypogastric nerves before bifurcation PAL; 2) preserve right femoral, genitofemoral nerves before right side PAL below inferior mesenteric artery (IMA); 3) preserve inferior mesenteric plexus (IMP), nerves connect renal plexus and IMP before middle PAL above/below IMA; 4) preserve left femoral, genitofemoral nerves before left side PAL above/below IMA.

Results: Patients of first and second groups were compared. There were significant differences in intraoperative outcomes: mean operative time - 358.1±62.6 vs 302.9±62.5, p=0.0001; mean operative blood loss - 417.4±205.8 vs 700.0±346.4, p=0.0001; mean volume of lymphorrhea - 3270.0±1936 vs 2170.4±2006, p=0.048. The mean time of lymphorrhea was no significant difference. No one patient among 43 women with NSPAL have asymptomatic para-aortic lymphocysts, frequency of lymphocysts in second group was 8.3% (p>0.05). Frequency of dilatation of renal pelvis and calices in NSPAL group was 11.6% and in second group - 37.5% (p< 0.05).

Conclusion: The PAL must be nerve-sparing, because the technique of NSPAL is associated with decreased operative blood loss, postsurgical complication.
Plenary Session on Cervical Cancer

**RATE OF VERTICAL TRANSMISSION OF HUMAN PAPILLOMAVIRUS FROM MOTHERS TO INFANTS**

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**Background:** In contrast to consistent epidemiologic evidence of the role of sexual transmission of human papillomavirus (HPV) in adults, various routes may be related to HPV infection in infants.

**Aims:** We have assessed the extent of HPV infection during the perinatal period, and the relationship between mode of delivery and vertical transmission.

**Methods:** A total of 291 pregnant women over 36 weeks of gestation were enrolled with informed consent. Exfoliative cells were collected from maternal cervix and neonatal buccal mucosa. HPV infection and genotypes were determined with an HPV DNA chip, which can recognize 24 types. The HPV-positive neonates were re-evaluated 6 months after birth to identify the presence of persistent infection.

**Results:** HPV DNA was detected in 18.9 % (55/291) of pregnant women and 3.4 % (10/291) of neonates. Maternal infection was associated with abnormal cytology (p = 0.007) and primiparity (p = 0.015). The infected neonates were all born to HPV-positive mothers. The rate of vertical transmission was estimated at 18.2 % (10/55) which was positively correlated with maternal multiple HPV infection (p = 0.003) and vaginal delivery (p = 0.050). The rate of concordance of genotype was 100 % in mother-neonate pairs with vertical transmission. The neonatal HPV DNAs found at birth were all cleared at 6 months after delivery.

**Conclusions:** Vertical transmission of HPV DNA from HPV infected mother to the neonate increased when the infant was delivered through an infected cervix. However, the absence of persistent infection in infants at 6 months after delivery may suggest temporary inoculation rather than true vertical infection.
Plenary Session on Cervical Cancer

EVALUATION OF P16\textsuperscript{INK4A} AS A BIOMARKER IN CERVICAL INTRAEPITHELIAL NEOPLASIA

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Aim: To predict high grade CIN using the biomarker p16\textsuperscript{INK4A}.

Objectives:

(1) To detect CIN using Pap, visual tests (VIA, VILI), colposcopy and biopsy.

(2) To determine expression of high-risk HPV 16 and 18 in screen positive women.

(3) To study the biomarker p16\textsuperscript{INK4A} by immunostaining.

Material and methods: Prospective longitudinal study conducted from November 2009 - April 2011. 1500 women were screened for cancer cervix using conventional Pap, VIA and VILI. Sensitivity, specificity, positive and negative predictive value were calculated individually, sequentially and in parallel. Those positive underwent HPV DNA PCR, colposcopy and biopsy. Cervical scrape taken from women who were HPV DNA +VE but normal at colposcopy. P16\textsuperscript{INK4A} expression in biopsy and cytology studied using immunohistochemistry and immunocytochemistry.

Results: Screen positives were 235; underwent HPV DNA PCR and colposcopy. Sensitivity, specificity, PPV and NPV of Pap with ASCUS as cut-off was 40\%, 99.25\%, 35.25\% and 99.39\%; VIA 60\%, 93.06\%, 8.03\%, and 99.56\% and VILI 80\%, 86.06\%, 5.4\% and 99.76\% respectively. Pap, VIA and VILI used in parallel improved sensitivity, specificity, PPV, NPV to 100\%, 85.18\%, 6.38\% and 100\%. Positive HPV test was seen in 20 (HPV 16 n=18, HPV 18 n=2). Colposcopic abnormalities were detected in 83 and biopsy proven CIN in 15. 20\% of CIN 1 and 75\% of CIN 2/3 showed P16\textsuperscript{INK4A} expression. Immunocytochemistry was negative in HPV DNA positives (n=12), who were normal at colposcopy.

Conclusions:

(1) PAP test and visual techniques are complementary.

(2) P16\textsuperscript{INK4A} can be used as a predictor of high grade CIN.
Plenary Session on Cervical Cancer

A PROPOSED NEW PATTERN-BASED CLASSIFICATION SYSTEM FOR ENDOCERVICAL ADENOCARCINOMA (EAC): IT’S IMPACT ON CLINICAL MANAGEMENT


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Background: The incidence of endocervical adenocarcinoma (EAC), specifically in young women, has increased in developed countries. The current management and treatment modalities include lymph node dissection (LND) based on the depth of invasion of tumor (DOI) and tumor size. However, irregular distribution and architecture of normal endocervical glands limit accurate assessment of DOI. In view of high negative rate of lymph node (LN) involvement in these patients (95%), we conducted an international multi-institutional study to evaluate more reliable pathological criteria which correlate with poor patient outcome and LN metastasis.

Methods: The study collated data from 12 international institutions. 360 cases with LND were identified (stage 1A1 to IVB). The new proposed system is based on the pattern of tumor invasion. Pattern A: well-demarcated glands, regardless of DOI, B: early stromal invasion from well-demarcated glands and pattern C: diffuse, destructive invasion.

Results: Patients' age ranged from 20 to 83 years (mean 44.9) with tumor size 0.5-65 mm (mean 21 mm). DOI ranged from 0.1 to >40 mm (mean 7.7 mm) and lymphovascular invasion (LVI) was present in 145 cases. (Table)

Conclusions: Based on the new proposed pattern, 22% of patients did not need LND (pattern A, all stage I disease). Pattern B, seen in 25% of the patients, rarely had LN metastases (0.5%) or recurrences (3%). Cases with pattern C showed 24% LN metastases and recurrence rate of 21%, and could benefit from LND.

Our proposed pattern-based method is reproducible and correlates well with patients' outcome.

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Stage I</th>
<th>Stage II-IV</th>
<th>Total LN</th>
<th>Pts with Pos LN</th>
<th>Recurrence</th>
<th>DOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current method</td>
<td>360</td>
<td>327(91%)</td>
<td>33(9%)</td>
<td>8187</td>
<td>53(15%)</td>
<td>43(12%)</td>
<td>18(5%)</td>
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<tr>
<td>Pattern A</td>
<td>79(22%)</td>
<td>79(100%)</td>
<td>0</td>
<td>1651</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Pattern B</td>
<td>91(25%)</td>
<td>89(98%)</td>
<td>2(2%)</td>
<td>2153</td>
<td>7(8%)</td>
<td>3(3%)</td>
<td>2(2%)</td>
</tr>
<tr>
<td>Pattern C</td>
<td>190(53%)</td>
<td>157(83%)</td>
<td>33(17%)</td>
<td>4383</td>
<td>46(24%)</td>
<td>40(21%)</td>
<td>16(8%)</td>
</tr>
</tbody>
</table>

[EAC, LN involvement]
Plenary Session on Cervical Cancer

HYPER RADICAL SURGERY OF STAGE IIB CERVICAL CANCER PATIENTS APPLYING THE LATERALLY EXTENDED PARAMETRECTOMY (LEP)

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Introduction: We report our experience - with a completed 5 years follow up - on 148 stage IIB cervical cancer patients operated with the laterally extended parametrectomy (LEP) procedure.

Methods: A prospective randomized study was carried out between 1996-2006 to evaluate the LEP-Wertheim operation with or without neoadjuvant chemotherapy. Where histology suggested tumor spread beyond the threshold of our surgery, adjuvant chemo-radiotherapy was advised. 5 years follow up was completed (without lost for follow up) for the whole cohort of patients.

Results: 86 (58%) of the 148 patients were treated without adjuvant therapy. Overall 5-years survival in this group of patients was 85% (72/85). For those patients who needed adjuvant treatment (62/148), 5 years survival was 65%. 5 years survival for the whole cohort of 148 patients was 76%. Neo adjuvant chemotherapy had no effect on survival (78% with and 75% without neoadjuvant) . Complications in 10% of cases necessitated a second operation.

Conclusions: Our results suggest, that in more than half of the stage IIB cervical cancer cases, surgery without adjuvant treatment could provide equal or better survival than any kind of multimodality treatment alternatives. In our series, neoadjuvant CMVB chemotherapy did not affect treatment outcome. LEP procedure should be considered a treatment option for stage IIB cervical cancer.
Plenary Session on Ovary and Late Breaking Abstracts

APPLICATIONS FOR ONCOLOGIC DRUGS-LESSONS FROM THE ONCOLOGIC DRUG ADVISORY COMMITTEE

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Objectives: To evaluate concerns addressed by the FDA Oncologic Drug Advisory Committee review (ODAC).

Methods: From 2001 to 2011, presentations and transcripts from ODAC sessions of drug license applications were reviewed. Comments and concerns from these sessions were extracted. Chi-squared test and logistical regression were employed by SPSS.

Results: Of the 44 drug license applications reviewed, the majority (75%, n=33) of applications were single-agent therapy, the remainder were combination therapy (25%, n=11). Of the clinical trials presented, 29 (66%) licenses were phase III trials, while 15 (34%) were phase II studies. 32 (73%) were for solid and 12 (27%) hematologic malignancies. 18% (n=8) were for leukemia, 16% (n=7) lymphoma, 11% (n=5) breast, 9% (n=4) prostate, 7% (n=3) brain, 7% (n=3) skin, 7% (n=3) lung, 7% (n=3) pancreas and 18% (n=8) were for other cancers. Nearly half (46%, n=20) of all applications were not approved. We then extracted the most common concerns addressed by the committee obtained from the transcripts of all rejected drugs. 65% were based on missing or inadequate data, 55% had concerns about excessive toxicity and 45% commented on the appropriate use of study endpoints. Other concerns include: study design, conduct and analysis (40%), inadequacies of sample size (30%), and concerns on radiological imaging (15%).

Conclusion: Based on the ODAC review of all rejected cancer drug applications, the most common concerns include missing or inadequate data, excessive toxicity, and inadequate study endpoints. Clinical researchers need to consider these FDA recommendations in the future design of clinical trials.
MOLECULAR ANALYSIS OF SEROUS OVARIAN CARCINOMAS ARISING ON A BORDERLINE BACKGROUND

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Serous ovarian cancers that are associated with borderline tumors are widely regarded as low-grade tumors characterised by Ras-pathway activation. By reviewing >1000 serous carcinoma cases (Australian Ovarian Cancer Study and Westmead) we identified 105 with adjacent borderline malignancy and conducted mutation (high resolution melting/sequencing of TP53, KRAS and BRAF or OncoMap screening for 1,216 cancer mutations, n=60) and copy number aberration (CNA; SNP arrays, n=36) analysis, including 8 ‘paired’ cases where the borderline and invasive components were analysed separately. Surprisingly, we found that the distribution of histological grade was approximately equal in our cohort (grade 1, 37%; grade 2, 30%; grade 3, 33%), despite the prevailing view that serous carcinomas arising on a borderline background are low-grade. We found that CNA were virtually identical between ‘paired’ borderline and invasive components suggesting they are not ‘collision tumors’. Mutations in invasive tumors were identified in TP53 (24/60, 40%) and Ras pathway genes (15/60, 25%) including KRAS and BRAF as well as NRAS. Unlike BRAF and KRAS, we found no NRAS mutations in serous borderline tumors (n=48), suggesting that NRAS may have a stronger influence on the development of frank carcinomas. The degree of CNA was associated with mutation and grade and we propose that serous tumors fall into two groups, or ‘molecular grades’ based on the extent of CNA and mutation (Fig 1). Our findings may have important implications for the clinical management of serous tumors with activation of the Ras pathway.

![Fig 1a](image-url)

Fig 1. Summary of grade, mutation and copy number aberration (qualitative score: ▪ high, □ low) for serous carcinomas with co-existing borderline tumors (n=36).
Plenary Session on Ovary and Late Breaking Abstracts

FIRST EFFICACY RESULTS FROM OCTAVIA: FRONT-LINE BEVACIZUMAB (BEV) COMBINED WITH WEEKLY PACLITAXEL (WPAC) AND Q3W CARBOPLATIN FOR OVARIAN CANCER (OC)

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Background: BEV given with front-line chemotherapy (q3w paclitaxel + q3w carboplatin) followed by BEV alone significantly improved progression-free survival (PFS) vs chemotherapy alone in the GOG-0218 and ICON7 randomised phase III trials in OC. The single-arm OCTAVIA study evaluated front-line BEV + wPAC + q3w carboplatin. Previously presented safety results [ASCO 2012] indicated that the regimen is tolerable with a safety profile consistent with the well-defined profile in phase III OC trials. Here we report final PFS and additional secondary efficacy results.

Methods: Patients with newly diagnosed OC (stage IIb-IV or high-risk stage I/IIa) received BEV (7.5 mg/kg, d1) + wPAC (80 mg/m^2 d1, 8, 15) + carboplatin (AUC6, d1) iv q3w for 6-8 cycles, followed by single-agent BEV q3w for up to 17 cycles (1 year) in total. The trial was designed to recruit a patient population similar to that in ICON7. The primary endpoint was PFS. Secondary endpoints included response rate, duration of response, overall survival and safety.

Results: Between Jun 2009 and Jun 2010, 189 eligible patients were enrolled (median age 55 years [range 24-79]; 74% ECOG PS 0; 80% stage III/IV; 65% serous; 71% optimally debulked). Patients received a median of 6 chemotherapy cycles and 17 BEV cycles. At the data cut-off (20 June 2012), disease had progressed in XX patients (YY%) and AA (BB%) had died. Median PFS was XX months (95% CI: YY–ZZ). The response rate was YY%. OS data are immature.

Efficacy results, available in September 2012, will be reported.
Plenary Session on Ovary and Late Breaking Abstracts

A RANDOMIZED, DOUBLE-BLIND PHASE 2 TRIAL OF MAINTENANCE SORAFENIB IN EPITHELIAL OVARIAN OR PRIMARY PERITONEAL CANCER


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Background: Primary treatment of ovarian cancer (OC) is cytoreduction with adjuvant platinum/taxane chemotherapy. One strategy to prolong disease control and survival is to administer maintenance therapy after achieving a complete response. Sorafenib, an oral multikinase inhibitor of the VEGF/Raf/MEK/ERK pathway, has shown activity in OC patients. We conducted a double-blind, randomized, placebo-controlled, phase 2 study to assess efficacy and safety of sorafenib maintenance therapy for OC.

Methods: Patients with epithelial OC or primary peritoneal cancer in complete remission after initial platinum chemotherapy were randomized to maintenance sorafenib 400 mg BID or placebo. The primary endpoint was progression-free survival (PFS).

Results: Of 246 patients randomized, 93% had OC. Baseline characteristics were balanced between treatment arms. There was no significant difference between sorafenib and placebo arms for PFS (hazard ratio 1.09; 95% CI 0.72-1.63), although there was a notable imbalance in censoring (Figure). The most common ≥Grade 3 adverse events (AEs) were hand-foot skin reaction (39% vs 0.8%, respectively), rash (14.6% vs 0%, respectively), and hypertension (8.1% vs 0.8%, respectively). More patients receiving sorafenib versus placebo required dose reductions, resulting in lower than planned median daily dose, and treatment with sorafenib was of shorter duration with more frequent discontinuations due to AEs (Figure).

Conclusions: Maintenance therapy with sorafenib 400 mg BID did not improve PFS. Efficacy may have been mitigated by sorafenib dose reductions and discontinuations secondary to toxicity. Maintenance therapy should balance the need for prolonged treatment with acceptable toxicity.
245 Patients

Randomization

123 sorafenib

- 17.6 median tx duration, wk
- 83 (67.5%) dose reduction
- 585 mg median daily dose

16 deaths
2 lost to follow-up
105 discontinued
46 (37.4%) AE
40 (32.5%) progression
17 (13.8%) consent withdrawn
2 (1.6%) other

Median PFS 386 days (95% CI 230-691)
39 PFS events
84 censored (20 at day 1)

123 placebo

- 51.9 median tx duration, wk
- 37 (30.1%) dose reduction
- 800 mg median daily dose

12 deaths
1 lost to follow-up
91 discontinued
8 (6.5%) AE
71 (57.7%) progression
7 (5.7%) consent withdrawn
5 (4.1%) other

Median PFS 478 days (95% CI 337-567)
68 PFS events
55 censored (2 at day 1)
PROMOTER METHYLATION STATUS OF HIN-1 AND CACNA1A ASSOCIATED WITH OUTCOMES OF OVARIAN CLEAR CELL ADENOCARCINOMA
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Background: This study is to analyze promoter methylation of various tumor suppressor genes in different types of ovarian carcinoma and to identify potential therapeutic targets of ovarian clear cell adenocarcinoma (OCCA).

Materials and methods: The promoter methylation statuses of 40 genes in primary ovarian carcinomas including 47 clear- and 63 non-clear-cell type tissues, 6 OCCA cell lines, 29 ovarian endometriotic cysts, and 31 normal controls were analyzed by methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA). The MS-MLPA results were correlated with clinicopathological features and outcomes of 47 OCCA patients. Functions of the target genes were further explored by Western Blot, apoptosis assay, and caspase-3/7 activity.

Results: Frequencies of methylated RASSF1A, CDH13, CACNA1A, HIN-1, and sFRP5 genes in OCCA tissues were significantly higher than those in non-OCCA cancerous tissues and benign endometriotic cysts. The expected 5-year PFS and OS for patients with methylated promoters of HIN-1 and CACNA1A genes were significantly worse than those for patients without methylated HIN-1 (28% vs. 54%, p = 0.047 for PFS; 30% vs. 62%, p = 0.002 for OS, respectively) and CACNA1A (30% vs. 63%, p=0.01 for PFS; 40% vs. 75%, p=0.02 for OS). When the HIN-1 gene was over-expressed in ES2 cells, a significant reduction in cell growth and induction of apoptosis, and increasing paclitaxel sensitivity by reducing phosphorylation of Akt were observed.

Conclusions: Methylation of HIN-1 and CACNA1A promoters are two novel epigenetic biomarkers associated with poor outcomes in OCCA patients. Ectopic expression of the HIN-1 gene increased paclitaxel sensitivity through Akt pathway.
Plenary Session on Ovary and Late Breaking Abstracts

THREE DISTINCT MOLECULAR SUBTYPES OF MUCINOUS OVARIAN CARCINOMA


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Introduction: Mucinous carcinomas (MC) are a rare subtype of ovarian carcinoma with specific molecular abnormalities. MC respond poorly to conventional chemotherapy and new molecular approach to classification and treatment is needed. Here we explore the relationship between HER2 amplification and activating KRAS mutation in MC of the ovary.

Methods: Tissue microarrays (TMA) of MC and mucinous borderline ovarian tumors (MBOT) were created from 2 centers. IHC, FISH, and CISH were used to determine HER2 status, and intratumoral heterogeneity. KRAS testing was done by Sanger sequencing.

Results: HER2 positivity was determined by IHC, FISH/CISH with a strong agreement (Kappa 0.95) and appeared to be near perfectly exclusive of activating Ras-pathway mutations. Our initial study revealed 6/20 HER2-amplified and 14/20 KRAS-mutant with 1 case having both abnormalities. These findings were validated in a completely independent series where 20/97 cases were shown to be HER2-amplified, 53/97 were KRAS-mutant, 4/97 cases had both a KRAS mutation and HER2 amplification, 27/97 cases revealed no detectable abnormalities.

Conclusions: HER2 amplification and KRAS mutations are both associated with activation of the Ras-signaling pathway. Mutually exclusive mechanisms of Ras-pathway activation are well described for other cancer types, including other ovarian cancer types (e.g. low-grade serous carcinoma). We propose that three major molecular subtypes of mucinous ovarian carcinoma exist i.e. those with HER2 amplification, KRAS mutation, and neither KRAS or HER2 abnormalities, and these may influence treatment decisions and novel targeted therapy development. Next-generation sequencing will allow comprehensive study of the double-negative and double-positive cases.
Plenary Session on Ovary and Late Breaking Abstracts

EFFECT OF BEVACIZUMAB (BEV) PLUS CHEMOTHERAPY (CT) FOR PLATINUM-RESISTANT RECURRENT OVARIAN CANCER (OC) WITH ASCITES: ANALYSIS OF THE AURELIA TRIAL

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Introduction: In AURELIA, adding BEV to CT significantly increased progression-free survival (PFS) vs CT alone in platinum-resistant OC (hazard ratio [HR] 0.48 [95% CI: 0.38–0.60]; p< 0.001). As VEGF expression correlates with ascites, we conducted exploratory analyses in the predefined subgroup of patients with ascites recorded in the eCRF at baseline.

Methods: Eligible patients in AURELIA had measurable/assessable OC that had progressed < 6 months after platinum-based therapy. Patients with refractory OC, a history of bowel obstruction or >2 prior anticancer regimens were ineligible. Investigators selected single-agent CT before randomisation to CT alone or combined with BEV until disease progression. The primary endpoint was PFS.

Results: Ascites were detected at baseline in 59/179 patients (33%) receiving BEV-CT vs 54/182 (30%) receiving CT alone in platinum-resistant OC (hazard ratio [HR] 0.48 [95% CI: 0.38–0.60]; p< 0.001). As VEGF expression correlates with ascites, we conducted exploratory analyses in the predefined subgroup of patients with ascites recorded in the eCRF at baseline. Among patients with ascites, 1/59 (2%) receiving BEV-CT vs 10/54 (19%) receiving CT underwent paracentesis during study treatment.

Conclusion: Despite their worse prognosis, women with ascites experienced clinically meaningful improvements in PFS with the addition of BEV to CT. These exploratory findings are consistent with results in the overall population. Moreover, the addition of BEV to CT allowed better control of ascites, requiring less paracentesis.
Plenary Session on Ovary and Late Breaking Abstracts

TOPOTECAN-CARBOPLATIN VERSUS STANDARD PLATINUM COMBINATIONS IN PATIENTS WITH PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER - THE GCIG INTERGROUP 'HECTOR' PHASE III TRIAL


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Background and aims: This randomized, multicenter NOGGO, AGO-Germany, AGO-Austria, GEICO intergroup phase-III trial was designed to test the efficacy and safety of the combination of topotecan with carboplatin (TC) compared with standard platinum combinations (SC) of gemcitabine-carboplatin, paclitaxel-carboplatin or pegylated liposomal doxorubicin-carboplatin in patients with platinum-sensitive recurrent ovarian cancer.

Methods: Patients with recurrence more than 6 months after first- or second-line platinum and taxane-based therapies were randomly assigned to TC (T 0.75 mg/m2 d1-3; C AUC 5 d1, q21d) or standard platinum combination for at least 6 cycles. The choice of standard combination was based on patient preference.

Progression-free survival rate at 1 year was defined as primary endpoint; secondary endpoints were toxicity, quality of life, median progression-free and overall survival.

Results: Between February 2007 and December 2009, 550 patients were randomized. A median of 6 cycles was administered in both arms. With a median follow-up of 20 months, PFS after 1 year was similar in both arms (37% in TC, 40% SC, p=0.47). Median PFS was 10 months for TC and 11 months for SC (p=0.41), median OS was 25 months and 31 months, respectively (p=0.16).

Most patients (68%) preferred gemcitabine-carboplatin as standard platinum combination, mainly based on expectation of a favourable non-hematologic toxicity profile. Response rates were similar in both arms, grade 3/4 hematologic toxicity was significantly higher in SC.

Conclusions: Combination therapy with topotecan-carboplatin did not improve outcome of patients with platinum-sensitive recurrent ovarian cancer compared to standard platinum combinations. Given the choice for standard combination, patients expressed a clear preference for gemcitabine-carboplatin.
Plenary Session on Ovary and Late Breaking Abstracts

IMPROVED EFFECTIVENESS IN OVARIAN CANCER SCREENING USING SERIAL TRANSVAGINAL ULTRASOUND-MORPHOLOGY INDEXING - INCREASED SURVIVAL, REDUCED FALSE POSITIVES & COST SAVINGS

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Background: Effective ovarian cancer (OVCA) screening should include: the predominant detection of early stage disease, improved survival, low false positives and favorable costs. We show that serial transvaginal ultrasonography (TVS) with morphology indexing reduces false positives, detects early stage disease, reduces mortality, and has cost savings from preventing progression.

Methods: 37826 women received 210426 screens from 1987-2011. Multiple comparisons in one-factor ANOVA were performed. Kaplan-Meier analysis evaluated survival with log-rank testing.

Results: Serial TVS with morphology indexing allowed many simple and complex TVS abnormalities to resolve even if they occurred as bilateral ovarian abnormalities and resulted in a PPV improved by ~2.9 fold to 23.3%. 51 screen-detected invasive OVCAs (23 Stage I (45%), 12 Stage II (24%) & 16 Stage III (31%)) were mostly aggressive type II malignancies (n= 44 (86.3%)) and had a 7 yr Kaplan Meier survival of 85.3 ± 0.5.6%. 82.9% (29/35) of early stage ovarian cancers detected by screening were aggressive type II ovarian malignancies. Overall screening performance improved over the period that serial TVS with morphology indexing was fully employed to Sensitivity/Specificity/PPV/NPV: 87.0%/99.7%/23.3%/99.99%. Using the average cost of treating Stage IIIC adjusted to 2011 dollars and the 35 early stage detections that screening prevented from progressing, the savings achieved through detecting early stage ovarian malignancies were favorably balanced against the costs associated with progression.

Conclusions: These screening efforts showed a shift to early stage detection of even aggressive type II malignancies with improved survival. Serial TVS with morphology indexing improved screening performance, especially the PPV. Cost analysis indicated that screening expenses were in balance with savings from preventing progression.
Plenary Session on Ovary and Late Breaking Abstracts

RISK OF EPITHELIAL OVARIAN CANCER IN ASYMPTOMATIC WOMEN WITH ULTRASOUND DETECTED OVARIAN CYSTS: A PROSPECTIVE COHORT STUDY WITHIN UKCTOCS

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Aim: To estimate risk of primary epithelial ovarian cancer (EOC) and slow growing Type I and aggressive Type II EOC in postmenopausal women with adnexal abnormalities on ultrasound.

Methods: Prospective cohort study in the ultrasound group of UKCTOCS of postmenopausal women with ultrasound detected abnormal adnexal (unilocular, multilocular, unilocular solid and multilocular solid, solid) morphology on their first scan. Women were followed up through the national cancer registries and postal questionnaires. Absolute risks (AR) of EOC and Type I/Type II EOC within 3 years of initial scan were calculated.

Results: Of 48230 women, 4367 (9.05%) had abnormal adnexal morphology. Median follow-up was 7.09 (25th Centile 6.03; 75th Centile 7.92) years. Forty-seven (32 Type I, 15 Type II) were diagnosed with EOC. The overall AR of EOC associated with abnormal adnexal morphology was 1.08% (95% CI: 0.79-1.43); 0.73% (95% CI: 0.5-1.03) for Type I; 0.34% (95% CI: 0.33-0.79) for Type II. In the subgroup (741) with solid elements (unilocular solid, multilocular solid and solid) overall AR was 4.45% (95% CI: 3.08-6.20), Type I 3.1% (95% CI: 1.9-4.6), and Type II 1.3% (95% CI: 0.6-2.4). 11982 women had both ovaries visualised and normal annual scans throughout the 3 year follow up period. In them eight Type II and no Type I cancers were detected.

Conclusions: Asymptomatic postmenopausal women, with ultrasound detected adnexal abnormalities with solid elements have a 1 in 22 risk of EOC. Despite the higher prevalence of Type II EOC, the risk of Type I cancer in women with ultrasound abnormalities seems to be higher than Type II. This has important immediate implications for patients with incidental adnexal findings as well as for any future ultrasound based screening.
Plenary Session on Ovary and Late Breaking Abstracts

SERIAL TUMOR MORPHOLOGY INDEXING PREDICTS RISK OF OVARIAN MALIGNANCY

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Background: Transvaginal sonography (TVS) is used to evaluate the risk of malignancy (ROM) for ovarian tumors. Morphology indexing (MI) incorporates ovarian volume and structure into an index score (0-10). For each MI score, our objective was to determine ROM and changes in MI over time for both non-malignant and malignant ovarian tumors.

Methods: 218,445 TVS screens were performed on 38,983 women from 1987-2012 in the Kentucky Ovarian Cancer Screening Program. For non-malignant tumors, the evaluation was limited to 1713 women (initial MI>0, multiple screens) who demonstrated resolution of MI over time. Tumors surgically removed or persistent on TVS were excluded from the non-malignant analysis. MI scores were also evaluated in 74 screen-detected ovarian malignancies. MI, change in MI (ΔMI), scan number to resolution, scan duration, and ΔMI per scan were analyzed.

Results: Eighty-five percent of malignancies detected on serial TVS had a MI≥5. The ROM increased with each rising MI score: MI=5 (2.7%), MI=6 (3.7%), MI=7 (12.6%), MI=8 (26.7%), MI=9 (27.8%), MI=10 (33.3%). Mean ΔMI decreased for all non-malignant tumors (minus 1.1 per scan), while mean ΔMI increased for all ovarian malignancies (plus 2.4 per scan). Non-malignant tumors resolved with 3 mean scans over an average of 6-12 months. On average, malignant tumors were followed with 2.1 scans over 2.3 months before surgical removal.

Conclusions: An increasing MI score correlates with a rising risk of ovarian malignancy. Furthermore, serial tumor morphology indexing may provide additional information to help differentiate benign from malignant ovarian tumors.
Plenary Session on Ovary and Late Breaking Abstracts

TRENDS IN THERAPY AND SURVIVAL OF ADVANCED STAGE EPITHELIAL OVARIAN CANCER PATIENTS IN THE NETHERLANDS

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Objective: The aim of this study was to describe trends in survival and therapy in advanced stage epithelial ovarian cancer (EOC) in the Netherlands and to determine if changes in therapy affected survival.

Methods: All EOC patients diagnosed in the Netherlands during 1989-2009 were selected from the Netherlands Cancer Registry. Differences in treatment over time were tested by the Cochran-Armitage trend test. Multivariable relative survival analyses were performed to test whether changes in treatment are associated with survival.

Results: 23,399 EOC patients were diagnosed, of whom 15,892 (67.9%) in advanced stage (stage ≥2b). In advanced stage patients, the proportion receiving (neo-)adjuvant chemotherapy and optimal debulking (residuals < 1cm) increased over time in all age groups. In elderly patients (≥75 years) a stable proportion (approximately 28%) did not receive any treatment. Five-year relative survival in advanced stage patients increased from 18% in 1989-1993 to 28% in 2004-2009. In the multivariable model survival improved over time (relative excess risk (RER) of 2004-2009 was 0.71, 95% CI 0.67-0.75 compared to 1989-1993). This RER attenuated to 0.85 (95% CI 0.80-0.90) and 0.91 (95% CI 0.83-0.99) with inclusion of treatment variables in the model (surgery with chemotherapy or optimal surgery with chemotherapy, respectively). This suggests that the improvement was mainly, although not entirely, caused by changes in treatment.

Conclusion: Treatment in advanced stage EOC patients in the Netherlands improved over the last two decades; more patients received (neo)adjuvant chemotherapy and underwent optimal debulking surgery. Changes in treatment led to partial improvement of survival in EOC patients.
Plenary Session on Uterine Cancer

CHARACTERIZATION OF SEROUS AND HIGH GRADE ENDOMETRIOID CANCER OF THE UTERUS USING IMMUNOHISTOCHEMISTRY

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Objective: The difference between serous (SC) and high grade endometrioid (HGEM) adenocarcinoma of the uterus is unclear. This study examined a large cohort of these cancers with the use of immunohistochemistry (IHC) to improve classification.

Methods: 164 cases of SC and 127 cases of HGEM from two large Canadian centres were analyzed. Clinico-pathologic characteristics and outcome parameters were collected and IHC for TP53, p16, ER, PR and ARID1A was performed on tissue microarrays.

Results: Age (67.5 vs. 65 years, p=0.048), stage (p=0.0006), and adjuvant chemotherapy (70% vs. 23%, p<0.0001) differed between SC and HGEM cohorts. Serous cancers were more likely to recur (p=0.0002), particularly at distant sites (p=0.0005), with decreased overall survival (OS) and progression free survival (PFS) (50.2% vs. 77.6% 5 year PFS, p<0.0001). On multivariate analysis histology, stage, and age at diagnosis were associated with overall survival. IHC revealed differences in PR, p16 and p53 expression (p<0.0001 for each) between SC and HGEM but only p53 expression within HGEM cancers was associated with changes in outcome. Null mutations (IHC=0) of p53 in HGEM was associated with lower PFS and OS (p<0.0001, PFS&OS) compared to wild type.

Conclusions: Although SC and HGEM are both considered to be aggressive cancers, this data shows that SC carries a poorer prognosis compared to HGEM. The association between null mutations for p53 in HGEM and decreased overall survival is an example of how IHC may allow stratification of risk groups and aid in individualizing therapy.
Plenary Session on Uterine Cancer

ABSOLUTE DEPTH OF MYOMETRIAL INVASION A BETTER PREDICTOR OF CLINICAL OUTCOME THAN PERCENTUAL DEPTH OF INVASION IN ENDOMETRIAL CARCINOMA PATIENTS

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Background: In endometrial carcinoma myometrial invasion is a well known predictor of recurrence, and important in the decision making for adjuvant treatment. According to the FIGO staging, myometrial invasion is expressed as invasion of more or less than 50 per cent of the myometrium (50%MI). It has been suggested to use the absolute depth of invasion (DOI), or the tumor free distance to the serosa (TFD).

Methods: All patients diagnosed with endometrioid endometrial carcinoma at the RUNMC, and the CWH from 1999-2009 were included. Histological slides were reviewed for histological type and grade, DOI, and TFD. After revision 335 patients were identified. DOI, TFD, and 50%MI were evaluated for prediction of clinical outcome and pathological characteristics.

Results: DOI, 50%MI, and TFD equally predicted high FIGO stage, cervical involvement, tumor grade 3, and lymphovascular space invasion. Lymph node metastases were predicted by DOI and TFD, and not by 50%MI. The prediction of recurrence was best performed by the absolute DOI when compared to 50%MI, area under the ROC curve of 0.722, and 0.673 respectively (p< 0.01). The optimal cut-off value for DOI was 3.75 mm. In a multivariable comparison of DOI, 50%MI, and TFD, DOI remained as predictor of progression-free survival (HR 1.11, 95%CI 1.07-1.16).

Conclusions: DOI has a better predictive and prognostic performance than TFD and 50%MI. Possibly, DOI should substitute 50%MI as measure to express myometrial invasion in daily clinical practice. More research should be performed to confirm these results favoring DOI, and to determine the best cut-off value.
Plenary Session on Uterine Cancer

LONG-TERM SURVIVAL AFTER RADIATION THERAPY FOR EARLY STAGE ENDOMETRIAL CARCINOMA:
THE OSLO STUDY REVISITED

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Introduction: The benefit of radiation in patients with early stage endometrial carcinoma is still
debatable. Data on long time risk conferred by radiation is scarce.

Aim: To study long-term survival and the risk of secondary cancer based on a previously published

Patients and methods: Between 1968 and 1974, we included 568 patients with endometrial cancer
FIGO stage I. After primary treatment with abdominal hysterectomy and bilateral salpingo-
ophorectomy patients were randomized to receive either vaginal radium brachytherapy followed by
external pelvic radiation 40 Gy (N=288) or brachytherapy alone (N=280). Data on survival and
incident secondary cancers were obtained by linkage to the Registry of Statistics Norway and Cancer
Registry of Norway. We used Cox proportional hazards model to estimate hazard ratios (HR) with
95% confidence intervals (95% CI). We also conducted analyses stratified by age groups.

Results: After median 21 (range 0-43.4) years of follow-up there was no significant difference in
overall survival or relapse free survival between treatment arms with HR of 1.12 (95% CI: 0.95-1.33)
and HR 0.88 (95% CI: 0.55-1.40), respectively. Patients treated with external radiation had
significantly lower risk of developing locoregional relapse (p< 0.001). However, women younger than
60 years had a significant poorer survival after external radiation (HR 1.36; 95% CI: 1.06-1.76). In this
patient group the risk of secondary cancer was significantly increased (HR 1.9; 95% CI: 1.23-3.03).

Conclusions: We observed no survival benefit of external pelvic radiation in early stage endometrial
carcinoma. In women younger than 60 years, pelvic radiation decreased survival, probably due to
increased risk of subsequent second neoplasms. Adjuvant external radiotherapy cannot be
recommended to this patient group. Those who have received such treatment might eventually benefit
from prolonged post treatment surveillance with respect to secondary cancer.
Plenary Session on Uterine Cancer

SUPPRESSION OF CARBONYL REDUCTASE 1 PROMOTES TUMORIGENESIS AND TUMOR-ASSOCIATED MACROPHAGE MIGRATION BY INDUCTION OF EPITHELIAL MESENCHYMAL TRANSITION

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Background: Carbonyl reductase 1 (CBR1) is an NADPH dependent monomeric enzyme. Recently immunohistochemical analyses revealed that decreased CBR1 expression was associated with poor prognosis in endometrial cancers. Epithelial mesenchymal transition (EMT) promotes invasion activities and is reported to be associated with poor prognosis in various cancers. Therefore, to investigate whether suppression of CBR1 induces EMT and has an effect on tumorigenesis.

Material and methods: Sense and antisense CBR1 cDNA were transfected into endometrial cancer cell line, SNGM, respectively. To investigate the cell function affected by CBR1, MTT assay, invasion assay, and zymography were performed. Expression of epithelial and mesenchymal markers concerned with EMT were examined. In vivo study, 5X10^6 of these transfected cells were injected into right subcutaneous tissues of 4 week-old-nude mice. Subsequent tumor proliferation in every group was observed for 8 weeks. Developed tumors were removed by autopsy and EMT markers and tumor-related macrophage (TAM) were investigated by immunohistochemistry.

Results: Suppression of CBR1 promoted cell proliferation, cell invasion activities, and induced EMT. The tumor volume and weight in CBR1 suppression group were large compared with those in the control group. The numbers of TAM in stromal tissues was many compared with those in the control group.

Conclusion: Suppression of CBR1 promotes cell invasion activities by induction of EMT and cell proliferation activities in vitro and in vivo. Furthermore, suppression of CBR1 may suppress anti-tumor effect and promote pro-tumor effect on TAM. Over-expression of CBR1 has a possibility to be a new molecular target therapy for endometrial cancers.
Plenary Session on Uterine Cancer

HIGH CORRELATION OF MOLECULAR TUMOR ALTERATIONS IN ENDOMETRIAL CURETTAGE AND HYSTERECTOMY-SPECIMENS IN PATIENTS WITH ENDOMETRIAL CARCINOMA

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Objective: Several molecular alterations in endometrial cancer have been identified as important prognostic factors. Few studies have investigated these molecular markers in pre-operative curettage specimens. This study aims to determine whether molecular analysis of the endometrial curettage tissues can accurately reflect the molecular alterations found in the subsequent hysterectomy specimens.

Method: Formalin fixed paraffin embedded curettage and hysterectomy tumour tissues from 48 patients (42 endometrioid carcinomas, EEC; 6 non-endometrioid carcinomas, NEEC) were selected. Expression of p53, PTEN and β-catenin was determined by immunohistochemistry. Tumour DNA was isolated successfully in 90% of patients. Allele-specific hotspot mutation analyses in kRAS and PIK3CA, sequence analysis of TP53 and microsatellite instability (MSI) analysis were performed.

Results: In EEC patients, loss of PTEN, of nuclear β-catenin and p53-mutant expression were found in 43%, 10% and 10%, respectively. Hotspot mutations for kRAS and PIK3CA were identified in 24% and 7%. As expected, no alterations were found in β-catenin, kRAS and PIK3CA in the NEEC patients, whereas a p53 mutant expression pattern was found in 83%. MSI was only seen in EEC (19%) and was mutually exclusive with p53 mutations. Concordance for PTEN was 90%, β-catenin 96%, p53 98%, kRAS 100%, PIK3CA 100%, and MSI 93% respectively.

Conclusions: The results suggest that performing immunohistochemical and DNA-based techniques to evaluate molecular alterations in pre-operative curettage specimens can be relevant for clinical decision making. The resulting molecular signature provides initial pre-operative diagnostic information for several oncogenic pathways, which may contribute to individualized treatment strategies for endometrial cancer.
Plenary Session on Uterine Cancer

COST EFFECTIVENESS OF TOTAL LAPAROSCOPIC HYSTERECTOMY: RESULTS FROM A PROSPECTIVE RANDOMIZED TRIAL COMPARING LAPAROTOMY WITH LAPAROSCOPY FOR ENDOMETRIAL CANCER

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Aims: To estimate the cost-effectiveness of Total Laparoscopic Hysterectomy (TLH) versus Total Abdominal Hysterectomy (TAH) for patients with endometrial cancer.

Methods: Between 2005 and 2010, 760 patients were enrolled in a multicentre, prospective randomized trial comparing Total Abdominal Hysterectomy (TAH) with Total Laparoscopic Hysterectomy (TLH) for early endometrial cancer (LACE Trial). The trial provided an opportunity to model the changes to total costs and health outcomes measured by quality adjusted life years (QALYs). All relevant costs were valued and included and QALYs estimated for the time period of the trial. All uncertainties were included and propagated forward to the conclusions.

Results: TLH caused higher surgery costs (+$510) but saved 3.55 in-hospital bed days. TLH was associated with a significant reduction in postoperative surgical complications resulting in total cost savings to health services of $3739 per case. TLH was associated with a gain of 0.11 QALYs over the time period of the trial. The net economic benefit was $33,780 per patient treated with TLH instead of TAH. This statistic includes the costs saved and the QALY gains are valued in dollar terms. Considering that 2000 patients are treated for uterine cancer every year in Australia, this will amount to a net economic benefit of $67.5 million per annum.

Conclusions: TLH saves costs and increases health benefits and should be considered to replace laparotomy for all standard hysterectomies. The extent to which the data gathered from this trial can be generalized to the Australian population.
Plenary Session on Uterine Cancer

A PHASE II TRIAL OF BRIVANIB IN RECURRENT OR PERSISTENT ENDOMETRIAL CANCER: A GYNECOLOGIC ONCOLOGY GROUP STUDY

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Purpose: Brivanib, an oral, multi-targeted tyrosine kinase inhibitor with activity against vascular endothelial growth factor (VEGF) and fibroblast growth factor receptor (FGFR) was investigated as a single agent in a phase II trial to assess the activity and tolerability in recurrent or persistent endometrial cancer (EMC).

Patients and methods: Eligible patients had persistent or recurrent EMC after receiving one to two prior cytotoxic regimens, measurable disease, and GOG performance status of ≤ 2. Treatment consisted of brivanib 800 mg orally daily until disease progression or toxicity. FGFR2 activating mutation status was assessed. Primary end points were progression-free survival (PFS) at 6 months and objective tumor response.

Results: Forty-five patients were enrolled. Forty-three patients were eligible and evaluable. Median age was 64 years, and prior treatment consisted of one or two regimens in 26 (60.5%) and 17 (39.5%) patients, respectively. Twenty-four patients (55.8%) received prior radiation. Adverse events were consistent with those expected with anti-VEGF therapy. No GI perforations but one rectal fistula were seen. Nine patients had grade 3 hypertension with one experiencing grade 4 confusion (PRES). Eight patients (18.6%; 90% CI 9.6-31.1%) experienced clinical responses (one CR and seven PRs; median response duration, 6.3 months), and 13 patients (30.2%; 90% CI 18.9-43.7%) were PFS at 6 months. Median PFS and overall survival were 3.3 and 10.7 months, respectively. Associations were observed between activating FGFR2 mutations and response.

Conclusion: Brivanib is reasonably well tolerated and worthy of further investigation based on PFS at 6 months in recurrent or persistent EMC.
Plenary Session on Uterine Cancer

IS THERE A COMMITMENT TO OFFER LYMPHADENECTOMY IN EARLY STAGE HIGH RISK ENDOMETRIAL CANCER? A PROSPECTIVE 18F-FDG PET/CT BASED ANALYSIS

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Background and aims: High risk clinical stage I endometrial cancer (grade 2 and deep myometrial invasion, grade 3, serous, clear-cell carcinoma) had 10-35% of nodal involvement. Lymphadenectomy is considered reasonable, although unnecessary in the vast majority of women. The purpose of this study was to evaluate the role of 18F-FDG PET/CT in the preoperative nodal metastases detection.

Methods: Prospectively, from January 2006 to December 2011, 86 high-risk clinical stage I endometrial cancer patients, underwent a 18F-FDG PET/CT scan followed by surgery, including systematic pelvic lymphadenectomy. From December 2010 the sentinel node (SN) mapping with 99mTc albumin nanocolloid and blue dye cervical injection was included in our clinical practise. 18F-FDG PET/CT images were analyzed and correlated to histological findings.

Results: Median number of dissected nodes was 29. Sixteen women had pelvic nodal metastases (18.6%), of which 12 detected by 18F-FDG PET/CT. On patient-based analysis, sensitivity, specificity, accuracy, positive predictive value and negative predictive value of 18F-FDG PET/CT in detecting pelvic LN metastases were 75.0% 98.6%, 94.2%, 92.3% and 94.5%, respectively. Two out 4 false-negative cases occurred after the introduction of SN mapping and both were micro-metastases identified only by SN ultrastaging.

Conclusion: 18F-FDG PET/CT is an accurate tool for the detection of nodal metastases. The high negative predictive value may be useful in selecting patients who might benefit from lymphadenectomy, minimizing operative and surgical complications. SN mapping increases the adequacy of staging, by the diagnosis of micro-metastases.
**Plenary Session on Uterine Cancer**

ANALYSIS OF UNSUCCESSFUL OUTCOME CASES AMONG 165 YOUNG PATIENTS WITH ENDOMETRIAL CANCER WHO RECEIVED FERTILITY-PRESERVING HORMONAL THERAPY USING MEDROXYPROGESTERONE ACETATE

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**Objectives:** We aimed to clarify retrospectively, the incidences of ineffective treatment, myometrial invasion, up-grading (grade aggravation), double cancer and metastasis in young patients who received fertility-preserving high-dose medroxyprogesterone acetate (MPA) therapy for endometrial cancer.

**Patients and methods:** We reviewed 165 patients with atypical endometrial hyperplasia complex (57 cases), or endometrioid adenocarcinoma G1 (104 cases), or G2 (4 cases), who were determined to neither have myometrial invasion nor extrauterine metastatic diseases. After 4 months oral administration of MPA 600mg/day, D&C was performed. When the pathological diagnosis revealed residual disease, an additional 2 months of oral administration and D&C was repeated. After disappearance of diseases, careful follow-up was performed every 3 months. We retrospectively analyzed clinicopathological findings in 40 patients who underwent hysterectomy.

**Results:** Median follow-up period was 37.5 months. Fourteen cases (8.5%) did not respond to MPA-treatment, and pathological CR rates were 96.5% in AEH, 89.4% in G1 and 100% in G2. Thirty-nine cases later became pregnant and experienced 35 deliveries. Pathological examinations revealed 12 cases (7.2%) of myometrial invasion, 6 cases (3.6%) of up-grading (AEH to G1: 3 cases, G1 to G2: 2, G1 to G3:1), 3 cases of peritoneal malignant lesions, 9 cases of double cancer and 3 cases of metastases. In addition, we experienced 4 cases who temporarily showed up-grading who eventually showed pathological CR without hysterectomy.

**Conclusions:** Prior to starting MPA therapy, we strongly recommend that gynecologic oncologists should accurately explain to patients about the possibilities of unsuccessful treatment effects, extrauterine metastasis, concomitant double cancer and up-grading.
Plenary Session on Uterine Cancer

QUALITY OF LIFE IN A RANDOMIZED LIFESTYLE INTERVENTION PROGRAM IN OVERWEIGHT/OBESE ENDOMETRIAL CANCER SURVIVORS

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Background: Overweight/obese women with early stage Endometrial Cancer (EC) are more likely to die from obesity related disease than EC alone.

Aims: To assess quality of life (QOL) outcomes after a behavioral, lifestyle-change based intervention program for overweight and obese EC survivors.

Methods: A prospective randomized trial of n= 75 overweight and obese women with early EC. Women were randomized to:

1) Survivors of Uterine Cancer Empowered by Exercise and Healthy Diet (SUCCEED) (LI), a 6-month lifestyle intervention consisting of nutrition, exercise and behavioral modification counseling; or

2) a usual care group (UC).

QOL was measured by FACT-G which included the domains of physical, social, emotional, functional well being and fatigue. Changes from baseline to 3, 6 and 12-months were compared using SPSS 20.0.

Results: Baseline demographics for the two groups were similar: LI group (n=41) age 57.3 (±8.7 (SD)), BMI 36.3(±5.5); UC group (n=34) age 59.2 (±10.9); BMI 36.9 (±9.2). No significant differences were found between groups at baseline for all FACT-G domains. Significant group differences were observed between LI and UC at 3-months (p=.008) in the fatigue domain and 6-months (p=.048) in the physical domain. There was a trend observed in the physical domain at 12-months (p=.061) between LI and UC groups.

Conclusion: SUCCEED improved FACT-G physical and fatigue domains initially in overweight and obese EC survivors; however, the clinical implications of these changes are unknown and require a more robust sample with longer follow-up periods.
Oral Presentation:  BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

VALIDATING A VERSION OF THE M.D. ANDERSON SYMPTOM ASSESSMENT INVENTORY (MDASI) FOR USE WITH OVARIAN CANCER PATIENTS

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Background: The MDASI was developed to capture common cancer symptoms from the patients’ perspective. We describe here the validation and sensitivity of a module of the MDASI to be used with patients having ovarian cancer, the MDASI-OC.

Methods: Module items were developed from 14 qualitative patient interviews. 128 patients with invasive epithelial ovarian, peritoneal or fallopian tube cancer treated at MD Anderson Cancer Center were recruited. Patients completed the MDASI-OC, socio-demographic questionnaires, FACT-O, and a global QOL item. Clinical data were extracted from patients’ medical records. Reliability was assessed using Cronbach’s alpha, construct validity was tested using exploratory factor analysis and sensitivity to clinical variables was tested.

Results: The sample was primarily white (85.2%), with a mean age of 57.5y (±12.7y), and had previously been treated with chemotherapy (75.0%) and/or surgery (93.8%). Approximately 30% reported disturbed sleep, fatigue, or numbness/tingling of at least a moderate severity (score ≥5 on a 0-10 scale) for the core items. Approximately 20% of patients reported back pain, feeling bloated or constipation of at least a moderate severity on the ovarian cancer specific symptoms. Factor analysis revealed 6 underlying constructs (pain/sleep; cognitive; disease-related; treatment-related; affective; GI-specific). MDASI-OC symptom and interference items had a Cronbach’s α-value of 0.90 and 0.89, respectively. The MDASI-OC was sensitive to symptom severity by performance status (p=0.009), QOL (p=0.002), and FACT-O scores (p< 0.001).

Conclusion: The 27-item MDASI-OC meets common criteria for validation and reliability, and is sensitive to expected changes in symptoms with differences in disease and treatment status.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

LONG-TERM OUTCOME AFTER NEOADJUVANT RADIOCHEMOTHERAPY IN LOCALLY ADVANCED NON-INFLAMMATORY BREAST CANCER AND PREDICTIVE FACTORS FOR A PATHOLOGIC COMPLETE REMISSION

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Background: A series of neoadjuvant radio-chemotherapy (NRT-CHX) in locally advanced non-inflammatory breast cancer (LABC) has now been updated with a follow up of more than 15 years. Long-term outcome data and predictive factors for pathologic complete response (PCR) were analyzed.

Patients and methods: 315 LABC patients were treated during 1991-1998 with NRT-CHX (50 Gy, electron boost to the breast and the supra-/infraclavicular lymph nodes in 214 cases). Chemotherapy was given prior to RT in 192 patients, and concomitantly in 113; 10 patients had no chemotherapy. The follow up ended in November 2011. Age, tumor grade, nodal, hormone receptor status, simultaneous vs. sequential CHX and the time interval between end of RT and surgery were examined.

Results: The total PCR reached 29.2 % with LABC breast conservation becoming possible in 50.8%. 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 to 0.99], p = 0.03) could be obtained. Importantly, a pCR was the strongest prognostic factor for long term survival (HR 0.28 [95% CI 0.19-0.56], p< 0.001).

Conclusions: A PCR identifies patients with a significant better prognosis for long-term survival. A long time interval to surgery increases the probability of a pCR after NRT-CHX.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

LOWER LIMB SWELLING AFTER GYNECOLOGICAL CANCER TREATMENT - EFFECT ON QUALITY OF LIFE AND DAILY LIFE FUNCTIONING

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Background and aim: Lower limb swelling (LLS) is a common condition but few studies have evaluated its consequences. We investigated the impact of LLS on sleep, sexuality and daily life activities among gynecological cancer survivors.

Methods: In 2006, 789 patients who in 1991-2003 received pelvic radiotherapy for a gynecological cancer at one of two university hospitals in Sweden were included in a population-based study. 478 matched control women were recruited from the Swedish Population Registry. They received a validated postal questionnaire including 351 questions covering symptoms from pelvic organs, lymphedema, quality-of-life, demographics and sexual functioning. They were also asked how these symptoms affected daily-life functioning.

Results: Participation was 78% for cancer survivors and 72% for control women, mean follow-up after radiotherapy almost 7 years. 218 (35%) cancer survivors reported LLS after pelvic radiotherapy. Gynecological cancer survivors with LLS reported a poorer overall quality-of-life (RR 1.4), less satisfaction with sleep (RR 1.3), a higher prevalence of fecal- and urinary urgency and incontinence, and more often interpreted symptoms as recurrence of cancer (RR 1.4) compared to survivors without LLS. Satisfaction with sexuality did not differ between groups. LLS reduced physical activity, ability to perform house work and partake in social activities. Thirty-one percent of the survivors had seen a healthcare professional due to LLS.

Conclusion: Gynecological cancer survivors with LLS reported a poorer overall quality-of-life, less satisfaction with sleep and a higher prevalence of fecal- and urinary urgency and incontinence compared to survivors without LLS.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

AGO-CARE 1 - A MULTICENTER RETROSPECTIVE STUDY ON ADJUVANT THERAPY IN LYMPH-NODE POSITIVE VULVAR CANCER


Background: Women with lymph-node positive vulvar cancer show unfavorable outcome. Improved treatment strategies are therefore needed.

Methods: Patients with primary squamous-cell vulvar cancer treated at 29 gynecologic cancer centers in Germany 1998-2008 were included in a centralized database and analyzed retrospectively.

Results: A total of 1637 patients were documented with a median follow-up of 121 months. 491 patients had lymph-node metastasis in the groins (N+). 214 N+ patients (43.6%) developed recurrent disease within a median of 21.4 months. 190 N+ patients (38.7%) died, median overall survival (OS) was 43.4 months, compared to 212 months for node-negative patients. An increasing number of metastatic lymph-nodes was associated with shorter OS: 169(34.4%) patients had 1, 101(20.6%) patients 2, 62(12.6%) patients 3 and 86(17.5%) patients >3 positive lymph-nodes, corresponding OS was 22.4, 17.2, 18.4 and 10.2 months, respectively (for 73 patients number of nodes was unavailable). 240 N+ patients were treated with adjuvant radiotherapy (85.8%) or radiochemotherapy (14.2%). Median OS in these patients was significantly longer (66.9 months) compared to N+ patients without adjuvant treatment (35.7 months), the corresponding hazard ratio (HR) was 0.72 (95% CI: 0.53-0.97, p=0.029). This impact on OS remained consistent in multivariate analysis adjusted for age, ECOG, UICC-Stage, grading, invasion depth and number of positive nodes (HR0.68, 95% CI: 0.49-0.94, p=0.020) and was observed irrespective of the number of affected nodes.

Conclusions: To this day, this is the largest multicenter study on vulvar cancer. Our findings strongly suggest that the unfavorable prognosis of patients with node positive vulvar cancer can be improved by adjuvant therapy irrespective of the number of affected nodes.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

LEARNING CURVE OF ROBOT-ASSISTED LAPAROSCOPY IN GYNECOLOGIC ONCOLOGY SURGERY: EFFECTS ON OPERATING TIME AND MORBIDITY

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Objectives: The aim of this study was to evaluate the learning curve in robot-assisted laparoscopy of a surgical team specializing in gynecologic oncology, by analyzing all interventions performed with this new approach since its first use in our facility.

Material and methods: The 225 first robot-assisted procedures performed by our team were included in this descriptive analysis. Clinical, intraoperative, and postoperative data of all surgeries were prospectively collected. Isolated and poorly reproducible procedures were excluded, so a total of 187 interventions were finally used to assess the learning curve. The main parameter used to evaluate learning was the overall rate of postoperative complications. The other parameters included operative time and number of pelvic lymph nodes removed. CUSUM statistical analysis was used to draw the learning curve. After determining the number of cases necessary for learning, a comparative analysis was conducted to compare the learning period to the efficiency period.

Results: Fifty cases were necessary to master postoperative complications. The operative time consisted of three phases: the learning phase, with a gradual decrease in operative time; the consolidation phase, steady; and the final phase, with the introduction of more difficult cases, the training of junior staff, and an increase in operative time. There was a growing trend in the number of nodes removed. Comparative analysis of the learning period (senior surgeons) and the efficiency period (with increasing involvement of junior staff) showed a significant evolution of procedures, and didn't reveal any difference in terms of complications (44% vs. 31%, non significant), or mean number of lymph nodes removed (12.3 vs. 13.2, non significant).

Conclusions: To master all procedures in the field of gynecologic oncology, learning robot-assisted laparoscopy requires an average of fifty cases. From this point, teaching junior surgeons is acceptable in terms of safety and quality of the procedures.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

SHOULD SYSTEMATIC INFRARENAL DISSECTION BE THE RULE IN LOCALLY ADVANCED CERVIX CANCER PATIENTS WITH NEGATIVE PARAORTIC PRETHERAPEUTIC PET IMAGING?

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Rationale: Locally advanced cervix cancer (LACC) have a 20-25% risk of paraaortic node involvement. Extended field chemoradiation is the usual management in this situation. Paraortic lymphadenectomy is the reference method to accurately predict node status at this level. However, it is admitted that node involvement progresses in a stepwise manner from the pelvis to paraaortic level. We wanted to test the incidence of isolated node metastasis above inferior mesenteric artery (IMA) in PET negative patient and define whether an inframesenteric or infrarenal dissection should be the rule.

Material and methods: Patients with negative PET at paraaortic level were offered an extraperitoneal infrarenal paraaortic lymph node dissection, except in case of carcinomatosis at initial diagnostic laparoscopy. All nodes were removed from both common iliac bifurcations up to the left renal vein. Node groups below and above IMA were sent to pathologist for a separate examination. This prospective study was approved by our local IRB and patient gave an informed consent.

Results: From 2010 to 2012, 153 stage IB2 to IVA LACC patients from 3 cancer centers, fulfilled the inclusion criteria. 21 had paraaortic involvement (13.2%) and 4 of them were exclusively located above IMA (19% of the pN1 group, 95% CI 3-31%). All of them were microscopic metastases.

Conclusion: Given the significant rate of skip metastases above IMA, an infrarenal dissection should remain the rule.
Oral Presentation:  BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

PILOT RCT TO EVALUATE PLASMAJET FOR PREVENTION OF LYMPHOCYST FORMATION FOLLOWING BILATERAL GROIN NODE DISSECTION (BGND) FOR VULVAL CANCER

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Introduction: Vulvar cancer is rare with approximately 1000 cases reported annually in the UK. Lymph node involvement is an important prognostic indicator. Vulvectomy and bilateral groin node dissection is the preferred surgical treatment for early disease increasing survival. However significant morbidity with lymphocyst formation and wound breakdown has been reported in > 50% of cases.


Materials and methods: Prospective crossover double blind pilot RCT in tertiary oncology centre. Following ethics committee approval, 18 patients recruited into study and PJ use randomised to one groin prior to surgery. PJ used at power setting of 40% between 5-11 minutes following node dissection.

Patient demographics, intra and post-operative data, daily drain outputs and groin wound healing recorded.

Results: 10/18 received PJ on the right side and 8/18 on left. Mean Patient age was 74.43(37-92) years. Daily drain output from PJ side was 20-100mls and 100-430mls on contralateral side. 7/18 patients developed lymphocysts on PJ side requiring subsequent drainage and 3/10 required VAC dressing for wound breakdown. 15/18 on the non-PJ side developed lymphocyst. 7/18 required re-admission and intravenous antibiotics for wound infection. Length of stay unaffected as each patient acted as their own control.

Conclusion: Our results suggest that use of PJ appears to reduce daily lymph drain outputs and lymphocyst formation. Ischaemia rates and wound infection were lesser on the PJ side. Long term follow-up data is awaited to assess lymphedema and recurrence rates.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

A DESCRIPTIVE STUDY OF LOWER EXTREMITY LYMPHEDEMA IN WOMEN UNDERGOING SURGERY FOR ENDOMETRIAL CANCER

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Background: In addition to hysterectomy and bilateral salpingo-oophorectomy, comprehensive surgical staging for endometrial cancer includes pelvic and para-aortic lymphadenectomy. Similar to other studies evaluating lymphedema, performing this lymphadenectomy increases the potential for lower extremity lymphedema; however the available data in endometrial cancer regarding prevalence and morbidity are limited.

Methods: We performed a descriptive, cross-sectional survey study of all patients who underwent surgery for endometrial cancer at a single institution from 2006-2008. Survey information included symptoms, management, and information regarding lymphedema. Clinical and surgical data, such as body mass index (BMI), age, surgical stage, were abstracted from medical records. Fisher's exact tests were used to assess the impact of lymphedema with clinical factors.

Results: Of the 519 patients identified, 305 (58.8%) responded to the survey. Sixty-eight (22.3%) patients reported a subjective diagnosis of lymphedema. The most commonly experienced symptoms included leg swelling, tightness and leg pain/tenderness and a majority (61.8%) stated it affected their daily activities. Exacerbating factors included prolonged standing, heat, and walking. The most effective therapies utilized included bandaging (76%), compression stockings (68%), massage therapy (56%), leg elevation (57%) and diuretics (51%). There was no association with lymphedema and BMI, age, race, tobacco use, or the number of lymph nodes removed. Regardless of diagnosis, a majority of patients preferred educational information on lymphedema prior to surgery.

Conclusion: The patient-reported incidence of lymphedema occurs in 1/5 of patients undergoing surgery for endometrial cancer. Efforts to obtain the true incidence, to improve education and management of lymphedema are warranted.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

VENOUS THROMBOEMBOLISM (VTE) PHARMACOLOGIC PROPHYLAXIS FOR GYNECOLOGIC ONCOLOGY PATIENTS: ARE THE CURRENT GUIDELINES ADEQUATE?


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Objective: Guidelines from ACCP, ASCO and NCCN recommend prophylactic anticoagulation for all hospitalized cancer patients to prevent venous thromboembolism (VTE). Current literature shows that only 30-50% of these patients receive recommended VTE prophylaxis. The objective of our study was to perform a quality improvement project to increase VTE pharmacologic prophylaxis rates by 15% among patients with gynecologic malignancies hospitalized for non-surgical indications.

Methods: A standardized VTE prophylaxis module was added to all order sets for non-surgical admissions. Outcome measures included: 1) number of admissions receiving pharmacologic prophylaxis within 24 hours of admission; and 2) number of VTEs diagnosed during hospitalization or within 30 days of discharge. Patients were excluded if they had an existing VTE on admission or a documented contraindication to anticoagulation.

Results: Our pre-implementation data included 100 consecutive patients admitted for non-surgical indications between 01/01/2011-02/28/2011. 53 patients (53%) were excluded due to existing VTE (n=29) or a documented contraindication (n=24). Our post-implementation data included 136 consecutive patients admitted between 06/15/2011-08/15/2011. 55 patients (40.4%) were excluded due to existing VTE (n=25) or documented contraindication (n=29). Administration of pharmacologic prophylaxis within 24 hours of admission increased from 24% to 93% (p< 0.05). However, VTE rates were higher in the post-implementation group (n=9, 11.1%) compared with the pre-implementation group (n=2, 4.3%) (p=0.10).

Conclusions: Our project improved pharmacologic prophylaxis rates from 24% to 93% among gynecologic oncology admissions for non-surgical indications. However, hospital-acquired VTE rates increased despite adherence with guidelines. These hypothesis generating data suggest existing guidelines may be inadequate for this high-risk population.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

TRAJECTORY OF PERFORMANCE STATUS AND SYMPTOM SCORES IN THE LAST SIX MONTHS OF LIFE IN GYNECOLOGIC CANCER PATIENTS

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Background: Ontario’s cancer system has implemented two standardized assessment tools to improve care. The Palliative Performance Scale (PPS) measures performance status and the Edmonton Symptom Assessment System (ESAS) measures severity of symptoms. This study describes the trajectory of scores 6 months before death in an outpatient gynecologic cancer population.

Methods: An observational cohort study was conducted between 2007 and 2010. Patients had cervical, ovarian, or endometrial cancer and required ≥1 PPS or ESAS assessment in the 6 months before death. Outcomes were the average PPS and ESAS scores per week before death.

Results: 795 (PPS) and 1,299 (ESAS) patients were included. The average PPS score started at approximately 70 and ended at 40, declining more rapidly in the last two months. For ESAS symptoms, nausea, anxiety, and depression scores remained stable over the 6 months in the mild range. Drowsiness, well-being, lack of appetite, and tiredness increased in severity over time, particularly in the two months before death. Pain appeared uniquely elevated in cervical cancer.

[Graph showing PPS score for all gynecologic cancer types]
Conclusion: Trajectories of performance status remained in the “transitional” phase until the last week of life. ESAS scores followed two patterns: increasing versus generally flat. Symptoms became moderate to severe earlier in the course of illness in gynecologic cancers and affected a larger proportion of the population as compared to the general cancer population examined in prior studies utilizing this database.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

INSULIN USE AND BREAST CANCER MORTALITY IN TAIWANESE DIABETIC WOMEN: A POPULATION-BASED PROSPECTIVE FOLLOW-UP STUDY

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Background: Whether insulin use can be a risk factor for breast cancer is not yet fully answered. We evaluated whether insulin use at a time when insulin analogues were still not yet available in Taiwan could be predictive for breast cancer mortality.

Materials and methods: A total of 48,416 diabetic women aged ≥25 years in a nationally representative cohort were followed from 1995 to 2006 for breast cancer mortality. Cox proportional hazards models were used considering the following independent variables: age, sex, diabetes type, diabetes duration, body mass index, smoking, insulin use, and area of residence. Insulin use was also considered for its duration of use < 5 years and ≥5 years.

Results: Age was a significant predictor in all analyses. Insulin use without considering its duration of use was associated with an insignificant 29% to 42% higher risk. The risk associated with insulin use < 5 years was close to unity while compared to non-users. However, insulin use ≥5 years might be associated with a significantly higher risk in models adjusted for various confounders. In the models adjusted for all confounders including age, diabetes type, diabetes duration, body mass index, smoking and area of residence, insulin use ≥5 years was associated with an approximately 90% higher risk with borderline significance (0.05< P< 0.1).

Conclusions: This prospectively follow-up study suggests that insulin use (mainly human insulin) for 5 years or more may be associated with a higher risk of breast cancer.
Oral Presentation: BREAST, SURGICAL TECHNIQUES, SYMPTOMS, VULVA/VAG

RISK ADAPTED THERAPY OF PREINVASIVE BREAST CANCER (DCIS)

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25% of new diagnosed Breast cancer (BC) are nowadays preinvasive breast cancer (Ductal Carcinoma in Situ /DCIS). Risk adapted therapy if DCIS is still a matter of debate. Randomised studies favored lumpectomy and radiation therapy as standard treatment (NSABP-B17, B24). Using comprehensive histological workup Silverstein and Lagios established the Van Nuys Prognostix Index as a possibility for selecting patients treatment according to their Risk for local recurrence after breast conserving therapy of DCIS. In the Breast Cancer Center Bayreuth a prospective study with risk adapted treatment of 246 DCIS treated from 1994 - 2010.

All patients were treated by segmental resection surgery with a comprehensive pathological work up of the surgical specimen and controlled by specimen radiography. Clear margins of 0.5 - 1.0 cm are chosen for the surgical margins. Three Risk Groups can be selected: Low Risk (Breast Conserving Surgery without Radiation), Intermediate Risk (Breast Conserving Surgery with Radiation), High Risk (Mastectomy).

- Breast conserving therapy was possible for 231 DCIS cases (94,3%).

- Low Risk (n=120; 52%) with 3,3% local recurrence
- Intermediate Risk (n=111; 48%) with 9,9% Local Recurrence
- High Risk (n=15), Local Recurrence 7%.
- Median Follow-up time is 80 months.

No deaths for all cases of DCIS with or without recurrence because of Breast Cancer.

Conclusion: Risk adapted therapy for DCIS after segmental Resection and comprehensive histological workup of the surgical specimen is a safe procedure with excelent follow up results of the therapy.
Oral Presentation: CERVICAL CANCER

TO OPERATE OR TO RADIATE: THE VALUE OF SUV-MAX IN PET-CT OF CERVICAL CANCER PATIENTS IN PREVENTING BIMODAL TREATMENT

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Introduction: In early stages of cervical cancer (IB-IIA), surgical treatment alone is usually the treatment of choice. However, some high-risk patients are referred for postoperative chemoradiotherapy, leading to increased morbidity. Maximal Standardized Uptake Value (SUV_max) is a PET-CT derived semi-quantitative measurement of FDG uptake in a defined lesion and may reflect tumor aggressiveness. The purpose of this study was to determine if preoperative high SUV_max values can be used for the selection of initial therapy, thus reducing the side effects resulting from bimodal treatment.

Methods: The PET-CT studies of 46 cervical cancer patients who underwent surgery were reviewed, and SUV_max data were collected. Statistical analyses were performed to determine the relationships between SUV_max values and clinical parameters, modalities of treatment, and outcomes.

Results: SUV_max was found to correlate with depth of tumor invasion (r=0.46, p<0.003). A statistically significant correlation was found between SUV_max and histological grade, with the mean and variance of SUV_max significantly lower for grade 1, as compared with grades 2 and 3 (mean 1.10, 11.06, and 8.88, and variance 3.57, 45.60, and 29.79, respectively; p<0.0001 and p=0.076). A possible SUV_max cutoff value of 10.08 was identified as a potential indicator of increased risk for receiving bimodal treatment, with a sensitivity of 61.5% and a specificity of 75.8%.

Conclusion: SUV_max can be used for differentiating early-stage cervical cancer patients who will need postoperative adjuvant treatment and therefore can serve as an additional modality to reduce the need for bimodal therapy in these patients.
Oral Presentation: CERVICAL CANCER

SMALL VOLUME STAGE 1B1 CERVICAL CANCER. IS RADICAL SURGERY STILL NECESSARY?
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Objective: Current surgical treatment of FIGO stage 1B1 cervical cancer is radical surgery. However, several reports have shown that for small tumours a more conservative approach can be as effective in terms of survival, whilst at the same time reducing the morbidity associated with removing the parametrium. The objective of our study was to report survival and obstetric outcomes following conservative management of small-volume stage 1B1 disease.

Methods: All patients with FIGO stage 1B1 cancer and estimated tumour volume of less than 500mm³ in a loop biopsy specimen were included in the study, irrespective of other histological characteristics. A second loop biopsy was performed to rule out residual disease in 79% of patients.

Results: Sixty two women were identified with a median age of 35 years (range 27-67). Median tumour length was 9.75mm (7.2-20) and median depth of invasion was 1.55mm (0.3-5). Thirty five women (56.4%) were treated with loop biopsy, whilst 27 (45.6%) had simple hysterectomy. Fifty seven women (92%) had pelvic lymphadenectomy and one positive node was recorded. After a median follow up of 56 months (16-132) no recurrence was noted. Seven full term pregnancies have been achieved. There were no preterm deliveries or mid-term miscarriages.

Conclusion: Cervical loop biopsy or simple hysterectomy combined with negative pelvic lymphadenectomy for small-volume stage 1B1 cervical cancer offers excellent prognosis in terms of survival. Postoperative morbidity is reduced and obstetric outcomes may be improved. Should these results be verified by further prospective studies, radical surgery for these women may be avoided.
Oral Presentation:  CERVICAL CANCER

MORE RADICAL SURGERY IN PATIENTS WITH RESIDUAL TUMOR AFTER (CHEMO) RADIATION FOR CERVICAL CANCER DOES NOT IMPROVE SURVIVAL

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Introduction: Routine hysterectomy after (chemo)radiation for cervical cancer showed not to improve survival. Previously, we observed that gynecologic examination with cervical biopsies after (chemo) radiation allows identification of cervical cancer patients with residual disease. However, in 50% of these patients type I hysterectomy did not prevent locoregional recurrence. Therefore, local treatment policy was changed to more extensive surgery after identification of vital tumor cells.

Aim: Evaluate efficacy of more radical hysterectomy after identification of residual disease in cervical cancer.

Methods: A retrospective cohort study of cervical cancer patients (FIGO stage IB1-IVa) treated with (chemo) radiation between 1994 and 2011. Patients underwent gynecologic examination 8 to 10 weeks after treatment. Cervical biopsies were taken from patients judged to be operable. In case of residual cancer, surgery was performed.

Results: 498 cervical cancer patients received primary (chemo) radiation. Median age 54 years (IQR:44-72 years), median follow-up 2.3 years (IQR:0.9-5.1). In 345 patients, a biopsy was taken. Vital tumor cells were identified in 85 patients (25%). Salvage surgery was performed in 62 patients (12 type I/II, 50 type III/IV). Complete remission (medium follow-up, 3.5 years, IQR:1.2-5.2) was achieved in 38/62 patients (61%). All patients with residual disease not undergoing operation died of progressive locoregional disease. More extensive surgery did not improve progression free survival, but gave more severe morbidity.

Conclusion: Gynecologic examination after (chemo) radiation allows identification of cervical cancer patients with residual local disease, of whom a significant proportion may be salvaged by surgery. More radical surgery did not improve survival.
Oral Presentation: CERVICAL CANCER

ROYAL COLLEGE OF RADIOLOGISTS UK AUDIT OF THE IMPLEMENTATION OF IMAGE GUIDED BRACHYTHERAPY FOR CARCINOMA OF THE CERVIX 2010/11

J. Forrest1, J. Clarke2, K. Drinkwater3, Clinical Oncology Audit Committee

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Introduction: Radical treatment of locally advanced carcinoma of the cervix involves concurrent chemoradiotherapy followed by intra-cavity brachytherapy. GEC-ESTRO and the RCR have published guidelines on implementing image guided brachytherapy (IGBT) and it is being introduced nationally.

Aims: To define national dose fractionation schedules for radical radiotherapy and compare with RCR and GEC-ESTRO guidelines and provide baseline information on the use of IGBT.

Methods: All UK radiotherapy centres were invited to submit data electronically on all patients receiving radical chemo-radiotherapy for locally advanced or medically inoperable cancer of cervix commencing treatment 1st November 2010 - 28th February 2011. Data was collected and analysed at the RCR using excel.

Results: 43/58 centres (74%) participated in this audit, 254 patients. FIGO stage was IB 16%, IIA 3%, IIB 45%, IIIA 5%, IIIB 19%, IVA 8%, IVB 3%. Mean age was 54 (range 22-86). Median overall treatment time was 44.5 days with 90% of treatments being completed within ABS guideline of 56 days. 98% (239/243) of “fit” patients received chemotherapy. 75% of centres used HDR, 1% PDR, 9% MDR (1.3Gy/hr), 10% MDR (1.7Gy/hr) 4% Unknown. Mean total dose of radiotherapy (EQD2 Gy 10) was 72.1Gy HDR, (interquartile range 69.4-75.8), 76.7Gy MDR (interquartile range 70.9-79.6) 84Gy PDR (range 73.9-90.6). Of 230 brachytherapy treatment 75 (33%) used X-ray planning, 133 (58%) IGBT of which 21% (44) used MRI atleast one fraction.

Conclusions: Most centres are using HDR brachytherapy with lower than recommended total radiotherapy doses. IGBT is being used in approximately 2/3 of treatments.
Oral Presentation: CERVICAL CANCER

MULTI-CENTER, RETROSPECTIVE STUDY OF INTERMEDIATE RISK FACTOR GROUPING IN FIGO STAGE IB-IIA POSTOPERATIVE CERVICAL CANCER PATIENTS (KGOG 1021)


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Objective: To establish a new model to select intermediate risk group of patients with cervical cancer according to the performance to predict recurrence after radical surgery.

Methods: Between April, 1998 and December, 2009, the medical records of 2,158 patients who had undergone radical surgery for stage Ib-IIa1 cervical cancer were reviewed retrospectively with collaborative efforts of 12 centers which were affiliated with Korea Gynecologic Oncology Group. We set sixteen models of selecting intermediate risk group; classic criteria which consists of two or more intermediate risk factors, Sedlis criteria which is also called GOG criteria, and newly suggested fourteen models made by various combinations of statistically significant univariate variables such as size varying 2 cm to 4cm, LVSI, DSI, adeno or adenosquamous carcinoma.

Results: Total number of patients enrolled was 2,158, stage 1B1 was 1659(75.9%), adenocarcinoma was 361(16.7%), and 177 patients(8.2%) recurred during follow-up period. Mean duration of follow-up was 64.2 months. The individual intermediate risk factors (i.e., TS 2cm, TS 3cm, DSI middle 1/3, DSI outer 1/3, LVSI) showed statistical significance in univariate analysis by disease free survival. By log-rank test, the Chi-square value of KGOG-5 model was 61.1524 (p< 0.001), which suggested that it performs best out of sixteen models (classic ; 14.5289, Sedlis ; 25.3506). The results of ROC analysis of these models showed that KGOG-5 performs better than classic or GOG criteria.

Conclusion: We developed a new model to select intermediate risk cervical cancer patients after radical surgery, which performs better than classic or GOG criteria.
Oral Presentation: CERVICAL CANCER

A COMPARATIVE STUDY OF LAPAROSCOPIC RADICAL HYSTERECTOMY WITH RADICAL ABDOMINAL HYSTERECTOMY FOR I-II STAGE CERVICAL CANCER

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Objective: To determine whether laparoscopic radical hysterectomy (LRH) is a feasible alternative to radical abdominal hysterectomy (RAH) for stage I-II cervical cancer.

Method: A retrospective study was carried out with 900 patients with FIGO stage I- II cervical cancer. 900 patients were divided into two groups: 571 patients underwent total laparoscopic radical hysterectomy and pelvic lymphadenectomy and 329 patients treated by abdominal operation between June 2009 and December 2011 in the same hospital.

Results: The mean age was 45.16±8.37 (20-73) years in laparoscopic group and 46.63±9.51 (25-78) years in abdominal group. The mean estimated blood loss in the abdominal group was significantly greater than that in the LRH group (697.56±481.75ml and 456.87±290.62ml). The mean operative time was shorter in the RAH group compared with the LRH group (237.61±62.56min and 272.60±62.47min). But operation time of last fifty LRH was 247.60±58.46min comparable to RAH. Extent of vaginal resection margins was longer and hospital stay was shorter in laparoscopic group. No statistically significant difference existed between two group with respect to pelvic lymph node count, frequency of lymph node involvement, adjuvant treatment and intra-operative complications. Median follow-up was 23 months for the LRH group and 24 months for the RAH group. There was no significant difference in survival rate between two groups (98.5% for LRH and 98.6%RAH).

Conclusions: The laparoscopic radical hysterectomy and pelvic lymphadenectomy is a useful alternative to radical abdominal hysterectomy patients who diagnosed with FIGO stage I-II cervical cancer. The benefits include less blood loss, shorter hospital stay, with comparable oncologic outcome.
Oral Presentation: CERVICAL CANCER

FACTORS ASSOCIATED WITH PARAMETRIAL INVOLVEMENT IN PATIENTS WITH STAGE IB1 CERVICAL CANCER: WHO IS SUITABLE FOR LESS RADICAL SURGERY?

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Objective: To detect the possible clinicopathologic factors associated with parametrial involvement in patients with stage IB1 cervical cancer and to identify a cohort of patients who may benefit from less radical surgery.

Methods: We retrospectively reviewed 120 patients who underwent radical hysterectomy and pelvic lymphadenectomy as treatment for stage IB1 cervical cancer. Preoperatively accessible factors including tumor size, invasion depth and lymphovascular space invasion (LVSI) were reviewed.

Results: Overall, 18 (15.0%) patients had parametrial tumor involvement. Tumor size larger than 2 cm, invasion depth greater than 1 cm, presence of LVSI, corpus involvement, and positive lymph nodes were statistically associated with parametrial involvement. Tumor histology and histologic grade had no significant effect on parametrial involvement. Multivariate analysis for other factors showed invasion depth greater than 1 cm (odds ratio 11.5, *p*=0.029), and corpus involvement (odds ratio 10.1, *p*=0.022), were significantly associated with parametrial involvement. A subgroup with tumor size smaller than 2 cm showed no parametrial involvement, regardless of invasion depth or presence of LVSI.

Conclusion: In the FIGO stage IB1 cervical cancer, the parametrial involvement was associated with other pathologic prognostic factors. Tumor size smaller than 2 cm showed no parametrial involvement, regardless of invasion depth or presence of LVSI. Invasion depth greater than 1 cm and corpus involvement were significantly associated with parametrial involvement in multivariate analysis. These finding may suggest that tumor size may a strong predictor of parametrial involvement in FIGO stage IB1 cervical cancer, which can be used to select a subgroup population for less radical surgery.
Oral Presentation:  CERVICAL CANCER

NOMOGRAM PREDICTION FOR OVERALL SURVIVAL OF PATIENTS DIAGNOSED WITH CERVICAL CANCER

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Introduction: Nomograms are predictive tools that are widely used for estimating cancer prognosis.

Aim: The aim of this study was to create a nomogram to predict overall survival (OS) in patients diagnosed with cervical cancer.

Materials and methods: Cervical cancer databases of two large institutions were analysed. A multivariable Cox regression model, describing the association between established prognostic parameters and OS was estimated. From this model, a nomogram was constructed and validated using bootstrap cross-validation.

Results: Mean 5-year OS rates for patients with International Federation of Gynecologists and Obstetricians (FIGO) stage IA, IB, II, III, and IV were 99.0%, 88.6%, 65.8%, 58.7%, and 41.5%, respectively. Based on previous studies FIGO stage, tumor size, age, histologic subtype, lymph node ratio, and parametrial involvement were considered as predictors for OS. The prognostic performance of the nomogram exceeded that of FIGO stage alone and the nomogram's estimated concordance probability was 0.794, indicating accurate prediction of OS.
Figure 1. Nomogram to predict 3-year and 5-year overall survival using six easily available clinical characteristics

Total Points 20 40 60 80 100 120 140 160 180 200 220 240 260
3-year survival 98 97 96 94 92 90 88 86 84 82 80 78 76
5-year survival 96 95 94 92 90 88 86 84 82 80 78 76 74

[Figure 1]
Conclusion: Based on six easily available parameters a novel nomogram to predict OS of patients diagnosed with cervical cancer was constructed and validated. The nomogram provides accurate individual prediction of patients’ prognosis and might be useful when deciding on follow-up strategies.
Oral Presentation: CERVICAL CANCER

EVALUATION OF HPV DNA TYPING IN SENTINEL LYMPH NODE AND PRIMARY LESION OF CERVIX IN PATIENTS WITH CERVICAL CANCER

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Objectives: The aim of this study was to analyze the HPV DNA types in both sentinel lymph node (SLN) and primary lesion of cervix in patients with cervical cancer.

Methods: 45 patients who underwent radical hysterectomy and pelvic lymphadenectomy with cervical cancer were enrolled in this prospective study. SLN and primary lesion of cervix were evaluated with microscopic pathologic examination as well as HPV DNA typing using HPV oligonucleotide microarray.

Results: HPV DNA types were successfully identified in all the 45 patients studied. Sentinel node detection and frozen biopsy were performed on all 45 subjects. There were 33 benign and 12 malignant cases on frozen biopsy. On permanent histopathological specimen, there were 31 benign and 14 malignant cases. In 31 out of 33 cases determined to be benign on the sentinel node frozen biopsy, there were no pelvic lymph node metastasis on the permanent pathology. In only 2 cases found to be benign on the sentinel node frozen biopsy, there were pelvic lymph node metastasis on the permanent histopathology. These results are statistically significant (p< 0.0001).

Conclusions: SLN detection and frozen biopsy make it possible to minimize the unnecessary extensive pelvic lymph node dissection during radical hysterectomy. HPV DNA typing as well as microscopic examination of SLN and primary lesion of cervix can be an important biological marker for recurrence in the near future.
Oral Presentation: CERVICAL CANCER

A PROSPECTIVE RANDOMIZED TRIAL FOR EVALUATION OF THERAPEUTIC EFFICACY AND SAFETY OF NERVE-SPARING RADICAL HYSTERECTOMY IN CERVICAL CANCER

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Objectives: This study aimed to evaluate the efficacy of nerve-sparing radical hysterectomy (NSRH) for reducing postoperative pelvic organ dysfunction, and therapeutic safety.

Methods: From April 2003 to November 2005, 91 patients with cervical cancer stage IA2-IIA were randomly enrolled in this prospective trial. We compared pre- and postoperative pelvic organ function by urodynamic study (UDS), anorectal manometry, and standard questionnaires for bladder, rectal, and sexual function. Extent of resected paracervical tissues were measured for evaluating radicality and number of nerve fibers in paracervix was also counted to define the adequacy of nerve-sparing. Therapeutic safety was evaluated by comparing recurrence and survival with long-term follow-up.

Results: There were no differences in clinicopathologic parameters between two groups. Number of nerve was significantly lower in NSRH than conventional RH (CRH) (13±9.3 and 37±17, respectively, p=0.002), and extent of resected paracervix was not different. Volume of residual urine and bladder compliance were significantly deteriorated until 12 months after the surgery in CRH group. In contrary, all parameters of UDS were recovered no later than 3 months in NSRH. Evaluations of subjective symptoms using standard questionnaires showed that long-term significant bladder, bowel, and sexual dysfunctions were higher in CRH than those in NSRH. The time taken to obtain a post-void residual urine volume of less than 50ml was 12.0±5d in NSRH group and was 19.5±15d in CRH group (p< 0.001). No significant differences in recurrence and survival could be found.

Conclusions: NSRH appears to be effective in reducing postoperative pelvic dysfunction and therapeutically safe procedure.
Oral Presentation: CERVICAL CANCER

CHEMOTHERADIATION VERSUS RADIOTHERAPY IN POSTOPERATIVE CERVICAL CANCER PATIENTS WITH POOR PROGNOSTIC FACTORS: A RETROSPECTIVE DUTCH MULTICENTRE STUDY

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Aim: Can we improve survival of patients after radical surgery in early stage cervical cancer with poor prognostic factors adding concurrent chemotherapy to radiotherapy versus radiotherapy only?

Materials and methods: A retrospective multicentre study was performed in 11 Dutch radiation oncology centres using Kaplan - Meier method with logrank test and Cox proportional hazard models. Eligible FIGO stage I patients were treated between 2000 - 2010; a radical hysterectomy and lymphadenectomy ≥ 8 lymphnodes (LN) removed; squamous-, adenosquamous-, adenocarcinoma, intermediate or high risk features (postoperative pathology report). The radiation dose: 45-50.4 Gy/5 X 1.8-2.0 Gy/week, a boost in case of microscopic tumor positive margins (external beam or brachytherapy), chemotherapy: weekly Cisplatinum 40mg/m2.

Results: Of the 348 eligible patients, 263 received radiotherapy only, 85 chemoradiation. Median follow-up: 47.5 months. 47 intermediate and 300 high risk patients, mean number of LN removed:20.187 ≥1 tumour positive LN, 97 microscopic parametral invasion. 5-years DFS: 68% and 79% for radiation and chemoradiation group, p=0.13.Significantly more patients receiving chemoradiation had high risk features (95% vs 84%, p=0.007) and a higher mean number of tumor positive lymph nodes (2.27 vs 0.84; p < 0.001). The only factor showing benefit for the addition of chemotherapy in multivariate analysis was tumor positive lymph node status (HR: 2.4 95%CI 1.1-5.1 p=0.02). There was no difference in grade 3-4 toxicity except for small bowel toxicity.

Conclusion: Postoperative Platinum based weekly chemotherapy combined with radiotherapy improves survival in FIGO stage I cervical cancer patients with tumor positive LN.
Oral Presentation: OVARIAN CANCER

GENOMIC EXPRESSION OF STEM CELL MARKERS IN ASSOCIATION WITH RECURRENT EPITHELIAL OVARIAN CANCER

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Objectives: To determine the genomic expression of stem cell markers associated with recurrent serous ovarian cancers.

Methods: Clinico-pathologic characteristics, outcomes, and genomic data were obtained from The Cancer Genome Atlas. Kaplan-Meier, t-test, and logistic regression methods were used.

Results: Of 257 patients, stage I-II vs. III-IV disease comprised of 21 (8%) vs. 245 (92%) of study group. The median and 5-year overall survivals were 49 months and 36%, with 41 months median follow-up (range: 4-152 months). The recurrence rates of stage I, II, III, and IV disease were 17%, 60%, 65% and 76%; (p=0.005). We then divided the group into those with no evidence of disease vs. those who recurred after treatment. There were no differences in age, rate of optimal cytoreduction and grade between cured vs. recurrent patients. The median survival of cured patients was 87 months vs. 44 months in those who recurred (p< 0.001).

Fifteen genes associated with cancer stem cells (CSC) were identified based on recent literature. Compared to those without any evidence of disease, those who recurred had higher expression of MUC4 (1.12 vs. 0.60; p=0.011) and ABCG2 (-2.2 vs. -2.43; p=0.022) whereas CD44 (-1.81 vs. -1.57; p=0.009) and NANOG (-3.97 vs. -3.63; p=0.001) were expressed at lower levels. On multivariate analysis, these CSC-associated genes remained as independent predictors for recurrence: ABCG2 (HR=1.68; p=0.016), MUC4 (HR=1.22; p=0.045), CD44 (HR=0.65; p=0.047), and NANOG (HR=0.51; p=0.001).

Conclusion: Our data suggest that genomic expression of cancer stem cell markers may be predictive of recurrent serous ovarian cancer.
Oral Presentation: OVARIAN CANCER

CA-125 IN OCEANS: PHASE 3 RANDOMIZED STUDY OF GEMCITABINE/CARBOPLATIN + BEVACIZUMAB (GC+BV) OR PLACEBO (GC+PL) IN PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER

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Objective: In a small number of patients with ovarian cancer treated with BV, the relationship between CA-125 and disease progression (PD) has been shown to be altered. We examined how CA-125 levels correlate with RECIST-defined PD in OCEANS.

Methods: The primary end point was investigator-assessed progression-free survival by RECIST. CA-125 analysis was an exploratory end point. Declaration of PD based on CA-125 levels was disallowed; however, levels were obtained every 9 weeks (coinciding with tumor assessment). An exploratory analysis of CA-125 PD vs RECIST PD was conducted in the intent-to-treat population. GCIG criteria were used to classify CA-125 PD.

Results: Overall, 64 of 484 patients (13%) had confirmed CA-125-defined PD as well as RECIST PD. In the GC+PL arm, 33 patients had CA-125 PD, 32 of whom also had RECIST PD and the median time from CA-125 PD to RECIST PD was 48 days. In the GC+BV arm, 37 patients had CA-125 PD, 32 of whom also had RECIST PD, and the median time to RECIST PD was 63 days. One (0.4%) patient in the GC+PL arm did not have RECIST PD despite confirmed CA-125 elevation vs 5 (2%) patients in the GC+BV arm.

Conclusions: The relationship of CA-125 to PD may be altered in BV-treated patients; if used alone, it could lead to determination of PD that is unconfirmed by RECIST or occurs earlier than RECIST-defined PD. These data support the further exploration of CA-125 vs RECIST-defined PD in BV-treated patients.
Oral Presentation:  OVARIAN CANCER

EARLY GENOMIC INSTABILITY IN TUBO-OVARIAN PRENEOPLASTIC LESIONS

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Introduction: Genetic instability plays an important contribution in ovarian carcinogenesis. We investigated the molecular mechanisms underlying the telomere shortening in early and pre-invasive stages of ovarian cancer, serous tubal intraepithelial carcinoma (STIC), precancerous serous tubal intraepithelial lesions (STIL) and ovarian dysplasia (OD).

Methods: 51 STIL and OD from prophylactic salpingo-oophorectomies with BRCA1 mutation, 12 STICs, 43 high-grade serous ovarian carcinoma and 36 non cancerous controls were laser-capture microdissected from formalin-fixed paraffin-embedded sections, analyzed by comparative genomic hybridization (array CGH) and for telomere length (using quantitative real-time polymerase chain reaction based on the Cawthon method). STIL, OD and STIC were defined by morphological scores and immunohistochemical expressions of p53, Ki67 and γH2AX.

Results: We found few subtle genomic alterations in dysplastic epithelium from STIL and OD in opposition to the more important genomic imbalances in STIC (most common regions with gain in chromosomes 19q, 16p, 12q, 10q and 11q and with loss in chromosomes 3q, 2q and 11q). The total number of genetic alterations was the highest in ovarian cancers. STIC had the shortest telomeres followed by STIL and OD (p< 0.007). Ovarian carcinoma had shorter telomeres than non cancerous controls (p< 0.01) but statistically longer than STIC, STIL and OD. We found also a statistical correlation between γH2AX expression and telomere shortening (p=0.0016).

Conclusions: These findings suggest that genetic instability occurs in early stages of ovarian tumorogenesis. STIC and non invasive lesions are probably an important step in early serous ovarian neoplasia.
Oral Presentation:  OVARIAN CANCER

NON-ASCITES FORMING ADVANCED STAGE SEROUS OVARIAN CANCER IS CHARACTERIZED BY A UNIQUE IMMUNE RESPONSE GENE PROFILE

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Background: High-grade serous ovarian cancer (HGSOC) is the most common subtype of ovarian cancer, with ascites a common presenting feature. Little is known of the mechanisms leading to ascites formation. Recent publications on gene expression profiles of HGSOC revealed at least four expression subtypes, suggesting that HGSOC is a heterogeneous disease; however, data on ascites production was not included.

Aim: To identify gene expression profiles in HGSOC that correlate with differential ascites production in search of possible targeted pathways for therapy.

Methods: Using an Illumina platform, we compared gene expression profiles of 11 snap-frozen primary tumors obtained from patients diagnosed with stage 3-4 HGSOC, who had substantial ascites, to 12 primary tumors obtained from patients who had minimal ascites. Significantly differentially expressed genes were used to compare to the TCGA expression subtypes.

Results: Using a t-test (p< 0.05) statistic with a 2-fold change cutoff between cases with high and minimal ascites, our dataset revealed 52 probes that were differentially expressed between groups. These probe sets reveal a striking difference, mainly in genes that regulate T cell function and antigen presentation that are less expressed in the high volume ascites group. Our low ascites volume group resembles the ‘immunoreactive’ subset of cases within the TCGA dataset; Immunohistochemical validation of selected gene products is ongoing.

Conclusions: These novel findings indicate that HGSOC associated with large ascites volumes suggest a suppression of immune response. These molecular signatures resemble subtypes of HGSOC identified in the TCGA dataset, suggesting that these are clinically relevant subtypes.
Oral Presentation: OVARIAN CANCER

SERUM CA-125 AND HE-4 VERSUS AN ULTRASOUND BASED PREDICTIVE MODEL TO ASSESS RISK OF MALIGNANCY IN WOMEN WITH ADNEXAL MASSES

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Background and aims: The identification of novel biomarkers led to the development of the Risk of Ovarian Malignancy Algorithm (ROMA) incorporating both HE-4 and CA-125 to predict malignancy in women with a pelvic mass. An ultrasound prediction model (LR2) by the International Ovarian Tumor Analysis (IOTA) study already outperformed CA-125. In this study we compared diagnostic accuracy of LR2 with ROMA.

Methods: This study included 360 women with a pelvic mass scheduled for surgery that were enrolled in a previous prospective trial. Expert ultrasonographers, general gynecologists and residents performed preoperative transvaginal ultrasound and serum biomarkers were taken prior to surgery. Accuracy of LR2 and ROMA was estimated at completion of this study and did not form part of the decision making process.

Results: A total of 216 women were diagnosed with benign disease and 144 women with malignancy. Overall test performance of LR2 (AUC 0.950) was superior to ROMA (AUC 0.893).

<table>
<thead>
<tr>
<th>Prediction model</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR+</th>
<th>LR-</th>
<th>DOR</th>
<th>AUC</th>
</tr>
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<tbody>
<tr>
<td>LR2 (cut off 10%)</td>
<td>0.94</td>
<td>0.82</td>
<td>5.19</td>
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<tr>
<td>ROMA (cut off 12.5/14.4)</td>
<td>0.84</td>
<td>0.80</td>
<td>4.22</td>
<td>0.20</td>
<td>21.17</td>
<td>0.89</td>
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[Overall test performance of LR2 versus ROMA]

Difference in AUC was 0.057 (95% CI: 0.024-0.089; P-value 0.0006). Similar results were obtained when stratified for menopausal status.
Conclusion: LR2 outperforms ROMA in the characterization of a pelvic mass in both pre- and postmenopausal women. These findings suggest that HE-4 and CA-125 do not play an important role in the diagnosis of ovarian cancer if ultrasonography is available.
Oral Presentation: OVARIAN CANCER

IS SALPINGECTOMY AN ACCEPTABLE ALTERNATIVE TO BILATERAL SALPINGO-OOPHORECTOMY FOR BRCA MUTATION CARRIERS?

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Objective: Risk-reducing bilateral salpingo-oophorectomy (BSO) is advised for women with BRCA mutations, but there are adverse consequences of premature menopause. The majority of BRCA-associated ovarian cancers likely arise in the fallopian tube, therefore salpingectomy may be an alternative to BSO. We compared the costs and benefits of salpingectomy to BSO among BRCA mutation carriers.

Methods: We developed a Markov Monte Carlo simulation model to compare 3 strategies for risk-reduction in BRCA+ women:

(1) BSO;

(2) bilateral salpingectomy, and

(3) bilateral salpingectomy with delayed oophorectomy.

Net health benefits were measured in years of life expectancy and quality-adjusted life expectancy (QALYs), and primary outcome was the incremental cost-effectiveness ratio (ICER). The model estimated the number of future breast and ovarian cancers and cardiovascular deaths attributed to premature menopause with each strategy.

Results: BSO was associated with the lowest number of breast and ovarian cancers and the highest life expectancy compared to the other two strategies. Bilateral salpingectomy yielded a higher quality-adjusted life expectancy than BSO, with a favorable ICER of $9,483 and $9,987 per QALY gained for BRCA1 and 2, respectively. Bilateral salpingectomy with delayed oophorectomy yielded the highest quality-adjusted life expectancy but an unfavorable ICER of $129,065 and $307,546 per QALY for BRCA 1 and 2, respectively.

Conclusion: BSO offers the greatest risk reduction for breast and ovarian cancer among BRCA mutation carriers. However, bilateral salpingectomy yields a higher quality-adjusted life expectancy and is a cost-effective alternative to BSO in BRCA mutation carriers. Delayed oophorectomy after salpingectomy is prohibitively costly.
Oral Presentation: OVARIAN CANCER

CYTOREDUCTIVE SURGERY IN RECURRENT OVARIAN CANCER. THE DESKTOP SERIES OF THE AGO STUDY GROUP, NOGGO, MITO, AGO-AUSTRIA, SGOG AND GINECO


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Background: Surgery in primary ovarian cancer (OC) for maximal cytoreduction is standard of care. However, the role of surgery in platinum-sensitive recurrent OC is less clear, especially:

(1) surgical aim,

(2) identification of potential candidates for surgery,

(3) improvement of prognosis.

Material and methods: Retrospective multicentre study for identification of surgical aim and hypothesis for a score identifying candidates for surgery (DESKTOP-I-trial). Subsequent prospective validation of the AGO-score (DESKTOP-II).

Results: The DESKTOP-I trial analyzed 267 patients. Complete resection (CR) was associated with significantly longer survival compared with surgery leaving any postoperative residuals [median 45.2 vs 19.7 months; hazard ratio (HR) 3.71; 95% confidence interval (CI) 2.27-6.05; P< .0001]. A hypothetical score predicting complete cytoreduction was developed. This score was deemed positive, if three factors were present:

(1) CR at 1st surgery,

(2) good performance status,

(3) absence of ascites.

The prospective DESKTOP-II trial screened 516 patients. 51% of them were classified as score positive; 129 patients with positive score and first recurrence underwent surgery. The rate of CR was 76% thus confirming the validity of this score regarding positive prediction of resectability in more than 2 out of 3 patients. Complication rate of secondary surgery was moderate: re-operations in 11%, perioperative mortality in 0.8% of the patients.

Conclusions: Patients with recurrent OC seem to benefit only from CR. The AGO-score is a useful tool identifying patients in whom CR is feasible. The third step of DESKTOP trials (DESKTOP-III) comparing chemotherapy/surgery versus chemotherapy alone in patients with platinum-sensitive relapsed OC is already recruiting patients.
Oral Presentation: OVARIAN CANCER

POPULATION-BASED TESTING FOR BRCA1/2 MUTATIONS DOES NOT CAUSE SHORT TERM PSYCHOLOGICAL HARM: RESULTS FROM A RANDOMISED TRIAL (GCAPPS)


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Objective: To evaluate the feasibility and psychological impact of a population-based approach to genetic testing for cancer predisposing mutations.

Methods: Design- RCT for testing BRCA1/2 genes (disease-model) in the Ashkenazi Jewish(AJ) community (population-model), with population-screening(PS), family-history(FH) arms. Inclusion-criteria:

(a) AJ ethnicity,
(b) age>18 years.

Exclusion-criteria:

(a) FDR BRCA carriers
(b) prior BRCA testing.

Recruitment- self-referral based, followed genetic counselling. All PS arm participants and those fulfilling standard criteria in FH arm underwent genetic testing. HADS, short HAI, MICRA and SF12 questionnaires assessed psychological and quality-of-life outcomes at baseline, 7-days and 3-mths after test result. A random-effects model evaluated the effect of genetic testing on outcome variables and group*time interaction represented effect of intervention between the two arms.

Results/findings: 1615 people registered, 1168 were counselled and 1034 randomised to PS(n=530) and FH(n=504) arms. 33% were men and 67% women. The group*time interaction effect showed no significant difference between FH and PS arms in change in HADS-total (p=0.11,7days; p=0.77,3mths), HADS-anxiety(p=0.07,7days;p=0.37,3mths), HADS-depression(p=0.29,7days;p=0.69,3mths), SF12-PCS(p=0.32,7days;p=0.53,3mths), SF12-MCS(p=0.35,7days;p=0.54,3mths), HAI(p=0.64,7days;p=0.79,3mths), MICRA(distress(p=0.20), uncertainty(p=0.72) and positive experience(p=0.06)) scores over time. Genetic testing showed no difference in these outcome variables between PS and FH groups over time. HADS-total, anxiety, depression; MICRA-distress, uncertainty (p< 0.0005) scores significantly decreased with time but Quality-of-life and HAI scores did not change with time. The associations detected between covariates of interest and psychological outcomes were comparable with normative data from other populations.

Interpretation/conclusions: There is no difference in short term psychological and quality-of-life outcomes between population-based and FH-based testing for BRCA gene mutations.
Oral Presentation: OVARIAN CANCER

WHOLE BODY DIFFUSION-WEIGHTED MRI FOR NON-INVASIVE STAGING AND OPERABILITY ASSESSMENT IN PATIENTS WITH OVARIAN CANCER

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Background and aims: CT and FDG-PET/CT lack sufficient accuracy for peritoneal staging; a diagnostic staging laparoscopy is the necessary clinical standard in addition to imaging for operability assessment. We aim to evaluate whole-body diffusion-weighted imaging (WB-DWI) for non-invasive staging and operability assessment in ovarian cancer patients.

Methods: Thirty-two patients with suspected ovarian cancer underwent 3-Tesla WB-DWI consisting of diffusion-sequences combined with T2- and contrast-enhanced T1-weighted imaging as anatomical background, as well as FDG-PET/CT in addition to clinical work-up. The accuracy of WB-DWI for primary tumor characterization and FIGO-staging was compared to CT and FDG-PET/CT with histopathology as reference standard.

Results and conclusion: WB-DWI showed 97% accuracy for primary tumor characterization, compared to 91% for CT and PET/CT and correctly identified 5/6 primary tumors of non-ovarian origin while CT and PET/CT identified 3/6 and 2/6, respectively. For FIGO-staging, WB-DWI (94%) showed significantly higher accuracy than CT (56%, p=0.0015) and higher accuracy than PET/CT (72%). WB-DWI demonstrated higher accuracy for detection of small bowel and colon serosal implants (90 and 76%, respectively) compared to CT (79 and 72%, respectively) and PET/CT (76 and 72%, respectively). WB-DWI was more accurate for identifying retroperitoneal lymphadenopathies (77%) compared to CT (58%) and PET/CT (53%) and showed excellent correlation with PET/CT for detection of extraperitoneal metastases (kappa=1.0). WB-DWI is a promising single-step diagnostic modality for characterizing and staging ovarian cancer. The improved accuracy of WB-DWI for detecting serosal and extraperitoneal metastases might reduce the need for surgical staging procedures in selected patients suspected for ovarian cancer.
Oral Presentation: OVARIAN CANCER

TUBAL EPITHELIAL LESIONS IN SALPINGO-OOPHORECTOMY SPECIMENS OF BRCA-MUTATION CARRIERS AND CONTROLS

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Objective: A precursor lesion for ovarian carcinoma, tubal intraepithelial carcinoma (TIC), has been identified in BRCA-mutation carriers undergoing prophylactic bilateral salpingo-oophorectomy (pBSO). Other lesions were also identified in fallopian tubes, but different terminology, interpretation, and lack of knowledge of normal epithelium, have hampered to unravel their possible role in carcinogenesis. The aim of this study is to classify tubal epithelial lesions in BRCA-mutation carriers and controls to enable comparison of prevalence, area of localization, and possible malignant potential.

Methods: Two hundred twenty-six BRCA1/2-mutation carriers were included; ovaries and fallopian tubes, embedded completely, were reviewed. Controls included 105 women who underwent BSO for non-malignant reasons. Tubal epithelial lesions included the following categories: hyperplasia, minor epithelial atypia, TIC, and invasive carcinoma.

Results: Tubal neoplasia was identified in 7.1% (invasive carcinoma, 0.9%; TIC, 6.2%) of BRCA-mutation carriers compared to none in controls ($p=0.004$, Fisher's exact test). Hyperplasia and minor epithelial atypia were identified in 41.6% BRCA-mutation carriers and compared to 58.1% in controls ($p=0.005$, Pearson's chi square). Invasive carcinoma and TIC showed preference for the fimbrial ends ($p=0.027$, Pearson's chi square), while hyperplasia and minor epithelial atypia displayed more variation in localization.

Conclusions: Invasive tubal carcinoma and TIC were limited to BRCA-mutation carriers, whereas hyperplasia and minor epithelial atypia were commonly found in both BRCA carriers and controls. It is suggested that hyperplasia and minor atypia represent variations of normal tubal epithelium instead of premalignant lesions. Furthermore, total salpingectomy is strongly recommended as most but not all TIC occurred in the fimbriae.
Oral Presentation:  OVARIAN CANCER

MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL PATTERN OF PRE-INVASIVE TUBO-OVARIAN LESIONS

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Introduction: Histopathological examination of material from prophylactic salpingo-oophorectomies (pBSO) performed in patients at genetic risk of ovarian cancer can reveal pre-cancerous ovarian dysplasia and serous tubal intraepithelial lesions (STIL). We sought to study the morphological features and immunohistochemical expression patterns of neoplasia-associated markers in pBSO in comparison with serous tubal intraepithelial carcinoma (STIC) and non-cancerous controls (nBSO).

Methods: Morphological and immunohistochemical expression patterns of Ki-67 (proliferation biomarker), p53 (key pathway of mullerian serous tumorogenesis), Bcl2 (anti-apoptotic), PAX 2 (related to the Mullerian duct), γH2AX (a marker of genomic instability) and ALDH1 (a stem cell marker) were blindly evaluated by two pathologists in 111 pBSO, 12 STIC and 116 nBSO.

Results: Morphological ovarian and tubal scores were significantly higher in the pBSO than in controls (8.8 vs 3.12, p< .0001, for ovaries and 6.54 vs 1.58, p< .0001 for tubes). Increased γH2AX expression was observed in the pBSO and STIC compared with controls whereas expression patterns of Ki67, p53 and bcl2 were low to moderate in the pBSO group. STIC overexpressed Ki67 and p53 while bcl2 expression was low. There was a loss of PAX 2 in cases of pBSO and STIC. ALDH1 expression was low in nBSO, high in pBSO and constantly low in STIC.

Conclusions: The morphological and immunohistochemical profile of STIL, ovarian dysplasia and STIC might be consistent with progression towards neoplastic transformation in the serous carcinogenesis sequence. ALDH1 activation in pBSO samples and its extinction in STIC should be considered as a target for prevention.
Oral Presentation: OVARIAN CANCER

SUPPORT OF THE 'FALLOPIAN TUBE HYPOTHESIS' IN A PROSPECTIVE SERIES OF RISK-REDUCING SALPINGO-OOPHORECTOMY SPECIMENS IN BRCA-CARRIERS

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Objective: To determine the prevalence, localization and type of occult (non)invasive cancer in risk-reducing salpingo-oophorectomy (RRSO) specimens in BRCA-carriers and women from negative tested families.

Methods: A consecutive series RRSO specimens of asymptomatic, screen-negative high-risk women was prospectively collected in our tertiary multidisciplinary cancer clinic from January 2000 until March 2012. All high-risk women in this study were genetically tested on BRCA-mutations. The strict surgico-pathological protocol comprised complete resection of the ovaries and fallopian tubes, and transverse sectioning at 2-3 mm (from 2006 the SEE-FIM protocol was implemented).

Results: 360 RRSOs were performed in 188 BRCA1-carriers, 115 BRCA2-carriers and 57 BRCA-negative women at a median age of 44.0 years. Four occult invasive cancers were detected in BRCA-carriers (1.3%, 95% CI 0.03-2.61), all in BRCA1-carriers >40 years of age. All cancers, of which two tubal and two ovarian cancers, were FIGO stage I/II. Three non-invasive serous intraepithelial carcinomas (STICs) were detected in BRCA-carriers (1.0%, 95% CI 0.00-2.10). In BRCA-negative women one STIC was found (1.8%, 95% CI 0.00-5.16), however she had a BRCA2 unclassified variant. Total follow-up after RRSO was 1,691 woman years, in which one BRCA1-carrier developed peritoneal cancer (0.3%, 95% CI 0.00-0.82).

Conclusions: A low prevalence of occult invasive cancer was found in young asymptomatic, screen-negative women at increased ovarian cancer risk undergoing RRSO. This study adds to the advice to perform RRSO in BRCA1-carriers before the age of 40. All (pre)malignancies derived from tubal epithelium, supporting the hypothesis of the fallopian tube as site of origin of pelvic high-grade serous cancer.
Oral Presentation: OVARIAN CANCER

MUTATIONAL PROFILING OF PAIRED PRIMARY AND RECURRENT OVARIAN LOW GRADE SEROUS CARCINOMAS

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Introduction: Ovarian low grade serous carcinomas (LGSC) are less clinically aggressive than high-grade serous carcinomas yet show poor response to conventional platinum-based chemotherapy in the neoadjuvant, adjuvant and recurrent settings. Limited mutational studies in primary or recurrent LGSC samples have revealed low numbers of somatic mutations, most frequently in KRAS and BRAF. In this study, we aim to (1) identify novel mutations in LGSC that could provide novel therapeutic targets, and (2) assess the stability of mutations over time.

Methods: 13 LGSC cases with available primary and recurrent paired samples were identified, and tumour cells isolated from FFPE sections. DNA was extracted and targeted bidirectional sequencing performed using the Ion Torrent AmpliSeq™ Cancer Panel. The presence/allelic frequency of predicted mutations were determined using the AmpliSeq™ Cancer Variant Caller.

Results: Sequencing of 3 LGSC sample pairs revealed a missense KRAS mutation (g.chr12:25,398,284C>A;p.12G>V) in one case consistent with previous studies. Notably, we observed a similar variant frequency in the primary (587/1098 reads, 53.5%) and recurrent (881/1669 reads, 52.8%) sample obtained from the same case. We also observed a non-synonymous mutation in VEGFR2 (g.chr4:5,597,2,974T>A; p.472Q>H), previously associated with imatinib response in CML patients, at a similar frequency in the primary (120/199 reads, 60.3%) and recurrent (314/523 reads, 60.0%) samples from a separate case. Sequencing of remaining tumour pairs and corresponding normal DNA is ongoing.

Conclusion: Preliminary analysis reveals that mutations in LGSC are stable over time, suggesting that either primary or recurrent samples could be used to identify potential therapeutic targets.
Oral Presentation: UTERINE CANCER INCLUDING SARCOMA

INFLUENCE OF LYMPH NODE STATUS AND SYSTEMATIC LYMPHADENECTOMY ON OVERALL SURVIVAL IN ENDOMETRIAL CANCER

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Objective: Low-risk patients and non-standardized lymphadenectomy (LND) have confounded prior studies addressing the role of LND in endometrial cancer (EC). We sought to determine the impact of a) positive node numbers, ratios and sites and b) systematic LND on longevity in EC patients at risk for lymphatic dissemination.

Methods: All cases of EC managed surgically from 1/99-12/08 were identified. Cases satisfying the recently validated Mayo low-risk criteria for lymphatic spread (< 1.5% risk) were excluded to generate the at-risk study population. Number of positive nodes/total number nodes examined defined lymph node ratio (LNR). Systematic LND was defined as ≥ 22 pelvic and ≥ 10 paraaortic examined nodes. Overall survival (OS) was estimated via the Kaplan-Meier method and compared using the log-rank test. Age-adjusted hazard ratios (HR) were determined. Two-sided p-values < 0.05 established significance.

Results: 932 consecutive at-risk EC cases were surgically managed during the study period. LND performed in 780 cases (83.7%) detected positive lymph nodes (LN+) in 170 (21.8%). Five-yr OS was 33.7% with LN+; 84.4% with negative lymph nodes (LN-) (p< 0.001). With both pelvic and paraaortic LN+, the 5-yr OS was 24.5% v. 40.2% and 44.5% for LN+ limited only to the pelvis or paraaortic area, respectively (p=0.04). Poorer OS was associated with both increasing number of LN+ (p< 0.001) and increasing LNR (p< 0.001; LNR 0, HR=1; 0.01-0.05, 3.41; >0.05-0.10, 3.69; >0.10-0.20, 8.29; >0.20-0.50, 13.40; >0.50, 15.50). Systematic LND significantly improved OS in LN+ cases: 5-yr OS was 46.2% following systematic LND; 21.5% after a less than systematic LND (p=0.003).

Conclusion: While the presence of LN metastases decreased OS, the performance of a thorough, systematic LND among those at high risk of death (LN+) improved OS. Whether improved survival is directly due to LND or secondary to LN+ specific adjuvant therapy warrants further investigation.
Oral Presentation: UTERINE CANCER INCLUDING SARCOMA

ANGIOTENSIN II TYPE I RECEPTOR AND MIR-155 IN ENDOMETRIAL CANCERS: SYNERGISTIC ANTIPROLIFERATIVE EFFECTS OF ANTI-MIR-155 AND LOSARTAN ON ENDOMETRIAL CANCER CELLS

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Introduction: MicroRNA-155 (miR-155) is one of the micro RNAs most consistently involved in neoplastic diseases, and it is known to repress the angiotensin II type 1 receptor (AGTR1).

Aim: To evaluate the expressions of miR-155 and AGTR1 and to clarify the potential efficacy of anti-miR-155, alone and in combination with AGTR1 blocker losartan in endometrial cancers.

Design: Expressions of miR-155 and AGTR1 were evaluated using real-time PCR and immunohistochemistry. An MTT assay was performed in endometrial cancer cells following anti-miR-155 and treatment with losartan, individually and in combination.

Results: miR-155 was over-expressed and AGTR1 was underexpressed in endometrial carcinoma tissues. AGTR1 immunoreactivity was found in six of ten (60.0%) normal endometrial samples, 11 of 14 (78.6%) endometrial hyperplasias, and 27 of 62 (43.5%) endometrial carcinoma tissues ($P = 0.051$), and patients with AGTR1 expression showed longer disease-free survival ($P = 0.019$). Abolishing the function of miR-155 and AGTR1 by anti-miR-155 or losartan inhibited cell survival of endometrial carcinoma cells; furthermore, combined treatment showed synergistic effects.

Conclusions: These results demonstrate that miR-155 and AGTR1 may be novel therapeutic targets in the treatment of endometrial cancers.
Oral Presentation: UTERINE CANCER INCLUDING SARcoma

A NEW TYPE ENDOMETRIAL CARCINOMA: ENDOMETRIOD HISTOLOGY WITH ATROPHIC ENDOMETRIUM AND POOR PROGNOSIS


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Background: Type I endometrial carcinomas are characterized by endometrioid histology (EEC), develop from hyperplastic endometrium, and have a good prognosis. Type II, or non-endometrioid carcinomas, arise in atrophic endometrium, and have a poor prognosis. However, about 20% of cases do not fit within this dualistic model and include EECs associated with recurrence, and possibly with atrophy. We aimed to evaluate grade 1 EEC with atrophic endometrium, a putative third type endometrial carcinoma.

Methods: Histological slides of all grade 1 EEC patients from the RUNMC and CWZ from 1999-2009, and from the Mayo Clinic from 2002-2008 were reviewed. Comparisons were made between patients with atrophic and hyperplastic endometrium.

Results: After review, 527 grade 1 EEC patients were identified. In 88 patients (16.8%) pre-existing endometrium was atrophic, 387 patients (73.3%) had hyperplastic endometrium. Fifty-two patients (9.9%) had proliferative endometrium or no pre-existing endometrium and were excluded. Atrophy correlated with older age, low BMI, advanced FIGO stage, malignant cells in peritoneal cytology, lymph node metastases, cervical involvement, lymphovascular space invasion, and deep myometrial invasion. Multivariable analysis showed that age (HR 1.06, 95%CI 1.01-1.12), FIGO stage (HR 8.47, 95%CI 1.73-41.57), and pre-existing endometrium (HR 3.11, 95%CI 1.11-8.70) were predictors of progression free survival.

Conclusions: Atrophic endometrium is an independent prognostic factor for patients with grade 1 EEC. EEC with atrophy may not follow the hypothesized progression model for type I tumors and may arise through unique carcinogenic pathways. Future research should investigate the carcinogenic pathways and response to treatment in this third type endometrial cancer.
Oral Presentation: UTERINE CANCER INCLUDING SARCOMA

DOES METFORMIN USE AMONG WOMEN WITH TYPE II DIABETES REDUCE THE RISK OF GYNECOLOGIC CANCERS?

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Objectives: Our objective was to determine if the risk of breast, endometrial and ovarian cancer in women with type II diabetes is lower among metformin users compared to diabetics who were managed without medication.

Methods: Female type II diabetic patients in a large U.S. managed care organization were identified from 1998 to 2006 and followed through 2009. Patients were stratified into the following treatment groups: metformin only, metformin+additional agents, non-metformin drugs, and no anti-diabetic medication. Study endpoints were cancer diagnosis, health plan disenrollment, death or study’s end, whichever occurred first. We conducted Cox proportional hazards models adjusted for age; race/ethnicity; comorbid conditions; and hormone replacement use.

Results: A cohort of 66,382 women met inclusion criteria and 1,684 cancers (1,291 breast, 300 endometrial and 93 ovarian cancer) were diagnosed during the 12 year follow-up period. Metformin in combination with additional agents (excluding insulin or sulfonylureas) reduced the risk of all cancers combined by 51% (HR=0.49; 95% CI: 0.41-0.59) compared to diabetic women who did not use anti-diabetic medications. Risk of endometrial cancer was 39% lower in this group (HR=0.61; 95% CI 0.40-0.93). Similarly, we found a 54% decreased risk of breast cancer (HR=0.46, 95% CI: 0.37-0.58). Due to the lack of events, no conclusions can be drawn concerning ovarian cancer risk. Metformin alone was not associated with reduced risk of any cancer but metformin+sulfonylureas (HR=0.64, 95% CI: 0.56-0.74) conferred protection against any cancer.

Conclusion: Use of metformin with other anti-diabetic therapy may reduce the risk of developing breast and endometrial cancer.
Oral Presentation: UTERINE CANCER INCLUDING SARCOMA

PREOPERATIVE SERUM CONCENTRATION OF HE4 AND CA12-5 IN PATIENTS WITH ENDOMETRIAL CARCINOMA

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Objective: To evaluate the performance of preoperative serum levels of HE4 and CA12-5 in predicting the presence of deep (≥50%) myometrial invasion and metastases in endometrial carcinoma.

Methods: Preoperative sera from 98 consecutive women diagnosed with endometrial carcinoma were collected. The concentrations of HE4 and CA12-5 were assessed by enzyme-linked immunosorbent assay (ELISA). The results were correlated to the histological grade and the presence of deep myometrial invasion and metastases found by aid of a surgical staging.

Results: Fourteen patients had metastases and 45 had a deep myometrial invasion. The concentrations of HE4 and CA12-5 were higher in the group with metastases than in the group without metastases (median [range], 148.6 pM [50.9-504.7 pM] vs. 77.2 pM [21.3-449.6 pM]; \( P = 0.001 \) and 20.0 U/mL [2.6-180.7 U/mL] vs. 4.3 U/mL [0.4-622.2 U/mL]; \( P < 0.001 \), respectively). The concentrations of HE4 and CA12-5 were also higher in the group with a deep myometrial invasion than in the group without invasion (median [range], 111.7 pM [21.3-784.1 pM] vs. 68.3 pM [24.7-140.3 pM]; \( P < 0.001 \) and 10.9 U/mL [1.5-622.2 U/mL] vs. 3.6 U/mL [0.4-49.2 U/mL]; \( P < 0.001 \), respectively). By multivariable analysis, HE4 level was the only predictive factor for the presence of metastases (OR, 1.010; 95% CI, 1.003-1.018; \( P = 0.008 \)) and HE4 and grade were the predictors for deep invasion (OR, 1.023; 95% CI, 1.009-1.037; \( P = 0.001 \) and OR, 1.776; 95% CI, 1.011-3.121; \( P = 0.046 \), respectively).

Conclusions: Of HE4 and CA12-5, particularly HE4 is associated with the presence of metastases and deep myometrial invasion in endometrial carcinoma.
Oral Presentation: UTERINE CANCER INCLUDING SARCOMA

OUTCOME OF FERTILITY PRESERVING TREATMENT IN PATIENTS WITH WELL-DEFFERENTIATED ENDOMETRIAL CARCINOMA AND SEVERE ATYPICAL HYPERPLASIA OF THE ENDOMETRIUM

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Objective: To evaluate the efficiency of progestin therapy on well-differentiated endometrial carcinoma (EC) and severe atypical hyperplasia of the endometrium (AH) and to assess the fertility outcome of the patients after treatment.

Methods: 44 patients (mean: 29 years) were entered to our study according to our criteria including 31 cases with EC and 13 cases with AH. After evaluation, all patients were treated by medroxyprogesterone acetate alone and received (f) D&C every 3 months to assess the response of treatment. The treatment will be terminated when the patients obtained complete remission (CR) or developed progressive diseases. Patients had follow-up regularly after CR and encouraged for pregnancy after 6 months follow-up of free of disease. ART will be performed in patients with infertility.

Results: Among 44 patients, 86.4% of patients had CR with 87.1% in EC group and 84.6% in AH group (p>0.05), but 13.6% of patients failed the treatment. Duration to achieve pathological response: 5.0±2.6 months in EC group and 4.7±2.5 months in AH group (p>0.05). 8 cases with recurrence detected in 34 (23.5%) patients who achieved CR and were followed up for more than 6 months. During the 47 months of follow up, there was no tumor related death with 100% survival rate. In 26 cases desired to be pregnant, 46.2 % got pregnancy with 26.9 % live birth rate. 41.7% cases obtained pregnancy by IVF-ET.

Conclusions: Progestin therapy is an acceptable option for young women with EC or AH to preserve fertility. Outcome of fertility after CR will be improved by IVF-ET.
Oral Presentation: UTERINE CANCER INCLUDING SARCOMA

METABOLIC TUMOR VOLUME MEASURED BY PREOPERATIVE 18F-FDG-PET/CT PREDICTS FOR RECURRENCE IN ENDOMETRIAL CANCER

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¹Obstetrics and Gynecology; ²Nuclear Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Republic of Korea

Objective: To evaluate whether metabolic tumor volume (MTV) and total lesion glycolysis (TLG) measured by 18F-FDG PET/CT have prognostic value in patients with endometrial cancer.

Methods: Between 2004 and 2009, 84 patients with endometrial cancer underwent preoperative 18F-FDG PET/CT at our institution. Patients' clinicopathologic data were reviewed from medical records retrospectively. We measured the SUVmax, SUVavg, MTV, and TLG of the primary tumor. Cox proportional hazards analysis were used to identify the predictors for recurrence.

Results: The median progression free survival (PFS) duration was 48 (1-85) months. There were 12 cases of recurrence. In univariate analysis, factors predicting for recurrence were myometrial invasion (P=0.012), lymphovascular space invasion (P=0.029), lymph node metastasis (P<0.001), non-endometrioid histology (p=0.002), advanced FIGO stage (p<0.001), MTV (p=0.001), and TLG (p=0.052). However, multivariate analysis showed that only lymph node metastasis (P=0.001, hazard ratio [HR] 9.286, 95% confidence interval [CI] 2.614-32.986) and MTV (P=0.009, HR 1.007, 95% CI 1.002-1.013) remained as independent risk factors for recurrence. The Kaplan-Meier survival graph showed that patients with a high MTV (≥17.15) had a significantly lower PFS rate than those with a low MTV (<17.15; p=0.034, log-rank test).

Conclusions: MTV measured by preoperative 18F-FDG PET/CT was an independent prognostic factor predicting for recurrence in endometrial cancer. This functional tumor parameter may be considered to plan further treatment and follow-up after operation.

<table>
<thead>
<tr>
<th>Total number of patients</th>
<th>84</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at diagnosis, year (range)</td>
<td>51 (24-76)</td>
</tr>
<tr>
<td>FIGO stage: I (%) II (%) III (%) IV (%)</td>
<td>58 (69.0) 11 (13.1) 13 (15.5) 2 (2.4)</td>
</tr>
<tr>
<td>Histology: Endometrioid (%) Papillary serous (%) Carcinosarcoma (%) Clear cell (%) Adenocarcinoma (%)</td>
<td>63 (75) 10 (11.9) 9 (10.7) 1 (1.2) 1 (1.2)</td>
</tr>
<tr>
<td>Grade: 1 (%) 2 (%) 3 (%)</td>
<td>31 (36.9) 25 (29.8) 28 (33.3)</td>
</tr>
<tr>
<td>Surgery: Hysterectomy+BSO (%) Hysterectomy+BSO+PLND (%) Hysterectomy+BSO+PLND+PALND (%)</td>
<td>5 (6.0) 28 (33.4) 51 (60.8)</td>
</tr>
<tr>
<td>Myometrial invasion &lt;1/2 (%) ≥1/2 (%)</td>
<td>56 (66.7) 28 (33.3)</td>
</tr>
<tr>
<td>Lymph node metastasis Absent (%) Present (%)</td>
<td>70 (83.3) 14 (16.7)</td>
</tr>
<tr>
<td>LVI Absent (%) Present (%)</td>
<td>63 (75) 21 (25)</td>
</tr>
<tr>
<td>Recurrence (%)</td>
<td>12 (14.3)</td>
</tr>
</tbody>
</table>

[Patients characteristics]
Fig. 1. Receiver operating curve (ROC) analysis for determination of the cutoff value of MTV predicting for recurrence. Area under the curve (AUC) for discriminating recurrence of MTV using the cutoff value of 17.15 was 0.679.

[Fig.1.]
Fig. 2. Progression-free survival (PFS) between the group according to MTV. There was statistically significant difference in PFS between patients with MTV ≥17.15 and MTV<17.15 (p=0.034, log-rank test).

[Fig.2.]
Oral Presentation: UTERINE CANCER INCLUDING SARCOMA

PROGNOSTIC VALUE OF PRETREATMENT CA125 LEVEL STRATIFIED BY AGE IN ENDOMETRIAL CANCER


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Background and aims: We aimed to investigate the outcome prediction of serum CA125 levels before definitive treatment and their correlation with other clinicopathological features in endometrial cancer.

Methods: A total of 773 cases with endometrial cancer and pretreatment serum CA125 levels treated between 2000 and 2010 were retrospectively reviewed. The correlation of clinicopathological characteristics, CA125 and treatment outcome was analyzed by independent sample t test, Chi-square test, and Cox proportional regression hazard model.

Results: A total of 285 (36.9%) patients were with serum CA125 greater than 35 U/mL before definitive treatment among 773 patients. Serum CA125 before treatment is highly correlated with advanced stage, non-endometrioid type cancer, high grade, deep myometrial invasion, presence of lymphovascular space involvement, adnexal or lymph node metastasis and positive cytology. By multivariate analysis, advanced stage (p < 0.0001), high grade (p = 0.003), and serum CA125 > 35 U/mL (p = 0.024) were independent risk factors in cancer specific survival (CSS). Using these three variables, three risk groups of low, intermediate, and high risk groups were classified into the death-predicting model. In the patients with age > 50 years, serum CA125 > 35 U/mL remained significant for CSS. In patients < = 50 years, serum CA125 was not significant using 35 U/mL as cutoff, while using 93 U/mL remained significant after adjusting confounding factors.

Conclusions: Pretreatment serum CA125, advanced stage and high grade are prognostic factors for endometrial cancer. Cutoff of serum CA125 at 93 U/mL in patients < = 50 years is preferred.
Oral Presentation: UTERINE CANCER INCLUDING SARCOMA

RELATIONSHIP BETWEEN THE HUMAN LEUKOCYTE ANTIGEN (HLA) CLASS I EXPRESSION AND THE PROGNOSIS OF ENDOMETRIAL CANCER

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Objective: Decreased human leukocyte antigen (HLA) class I molecule occurs frequently in many cancers and this abnormality might adversely affect on the clinical course of cancer. The present study was undertaken to investigate the relationship between immunohistochemical expression patterns of HLA class I and prognosis of uterine endometrial cancers.

Materials and methods: We studied 100 patients who had undergone hysterectomy, pelvic and paraaortic lymphadenectomy for endometrial cancers without pretreatments. Immunohistochemical study was performed to examine the relationship between HLA class I expression patterns, clinico-pathological characters, and its prognosis. The HLA class I expression patterns were classified into two groups (Positive and Negative pattern). HLA class I expression was composed of HLA class I heavy chain (HC-10) expression and b2-microgloblin (b2-M) expression. The cases, which both HC-10 and b2-M are strongly stained, are defined to be HLA classs I Positive pattern and any deviation from that was defined to be HLA class I Negative pattern.

Results: The Negative expression pattern of HLA class I in the primary lesions were strongly associated with FIGO stage III and IV (p< 0.001), lymph vascular space involvement (p=0.002), low histological grade (p=0.027), and the incidence of lymph node metastasis (p=0.004). Moreover, this pattern showed lower progression free survival rate than that of Positive pattern (p=0.008).

Conclusion: These findings suggest that negative expression of HLA class I can be an useful marker in poor prognosis in endometrial cancer.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

ISOLATED GROIN RECURRENCE IN RELATION TO LOW NODE COUNT IN SQUAMOUS CELL CARCINOMA OF THE VULVA

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Objective: To determine if low node count in inguinofemoral lymphadenectomy (IFL) in primary squamous cell carcinoma (SCC) of the vulva correlates with isolated groin recurrence in patients without adjuvant radiotherapy.

Methods: A multicenter retrospective review of patients with node negative SCC of the vulva, who underwent an IFL. Patients with and without isolated groin recurrences were identified and compared to identify risk factors. A multivariate analysis was conducted; p value of < 0.05 was considered significant.

Results: A total number of 113 patients was eligible for the analyses:109 patients underwent IFLs in 202 dissected groins and developed no isolated groins recurrences (median number of nodes per groin was 9 (range:1-38)), while four patients developed isolated groin recurrences (one patient with the recurrence in the non-operated contra lateral groin). Analyses were done on the three patients with a recurrence in the previously operated groin: five, eight and eight nodes were removed. Isolated groin recurrences were related to a node count < 10 (p=0.006), tumor stage (p=0.05) and differentiation grade (p=0.01), while there was no association with tumor localization (central/lateral), tumor diameter, multi-focality, depth of invasion or age at primary treatment.

Conclusion: The risk of developing an isolated groin recurrence after a negative inguinofemoral lymphadenectomy in patients with vulvar SCC is very low (2.65%). We found a significant relation between isolated groin recurrences and a node count less than 10 lymph nodes. A large well described patient cohort study is needed before clinical conclusions can be drawn.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

PATHOLOGIC FACTORS ASSOCIATED WITH GROIN NODE METASTASIS IN A POPULATION-BASED COHORT OF VULVAR CANCER PATIENTS

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Objective: To describe the pathologic factors associated with groin node metastasis in a population based cohort of vulvar cancer patients.

Methods: All cases of vulvar carcinoma diagnosed between 1998 and 2007 were identified using the provincial cancer registry. All pathology reports available from the registry for this cohort were abstracted for tumor details and prognostic factors. This analysis includes patients with vulva specimens greater than 1.5 cm labeled as “resections” and a groin node biopsy/resection within 6 months of each other. Univariate analysis was completed to determine pathologic factors of the primary vulvar tumor associated with groin node metastasis.

Results: We identified 1,254 patients using electronic registry records. Preliminary analysis indicates 292 patients had a vulvar resection and a groin node biopsy or resection within 6 months of each other. 130 (44.5%) had positive inguinal nodes. Pathologic factors in the primary tumor that were found to be associated with groin node metastasis included: depth of invasion (OR 1.07, CI 1.01-1.13; p=0.013); tumor thickness (OR 1.06, CI 1.01-1.11; p=0.03); presence of lymphvascular invasion (LVSI) (63.3% vs 36.0%, p=0.0004); grade (p=0.006); and tumor size > 2 cm (51.1% vs 25.7%, p=0.0002).

Conclusions: This large population-based cohort of vulvar cancer patients demonstrates that the pathologic factors depth of invasion, tumor thickness, presence of LVSI, grade, and tumor size are significantly associated with groin node metastasis. Reporting of these variables in the primary vulvar tumor is important for predicting likelihood of metastatic disease and influences treatment decision-making.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

SINGLE-PORT LAPAROSCOPY AND EXTRAPERITONEAL PARA-AORTIC LYMPHADENECTOMY: A SERIES OF THIRTY-TWO CONSECUTIVE CASES

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Objective: To report the technique and feasibility of single port extraperitoneal para-aortic (PA) lymphadenectomy in initial staging of patients with locally advanced cervical cancer.

Methods: Prospective study of patients with stage IB1N+-IVA cervical cancer treated at the Institute Gustave Roussy from 01/2011 to 03/2012. A single 2-3 cm left iliac incision was made perpendicular to a point situated 2/3 along the line drawn from the umbilicus to the anterior superior iliac spine. In the absence of peritoneal or ovarian spread, PA lymphadenectomy was performed via a left-sided extraperitoneal approach. The nodal tissues were dissected away from the aortic bifurcation to the left renal vein. Conventional instruments were used in all cases.

Results: Thirty-two consecutive patients with cervical cancer underwent a pretherapeutic laparoscopic staging procedure. No patient had PA FDG uptake on PET/CT. In one case lymphadenectomy was not feasible because of vascular anomalies of the renal vessels (low insertion of 2 left renal arteries). In this case, only 2 nodes were removed. No major perioperative complication occurred. No conversion to laparotomy or to conventional multiport laparoscopy was required. The median operative time was 190 min (range, 135-250). The mean and median number of lymph nodes removed were 18.6 and 17 [range, 2-47]. The definitive pathological analysis revealed that five patients (15.6%) had PA metastatic disease. This procedure did not result in any delays to planned concomitant radiochemotherapy.

Conclusions: This series reports that PA lymphadenectomy via the extraperitoneal approach with a single port using conventional instruments is feasible and safe.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

NEoadjuvant CHEMOTHERAPY IN LOCALLY ADVANCED VULVAL CANCER: DOES IT REDUCE SURGICAL MORBIDITY?

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Background: Management of locally advanced vulval cancer is complex and may involve mutilating surgery including exenteration. We investigated whether neoadjuvant chemotherapy (NACT) with cisplatin (50-80mg/m²)/5-fluoruracil (750mg/m² D1-4) would permit less aggressive surgery and/or avoid exenteration in patients with very advanced disease.

Methods: Retrospective data was obtained from records of women with stage 2-4 squamous cell carcinoma of the vulva who were planned to undergo 3-6 cycles of NACT followed by surgical resection from January 2001 to December 2010.

Results: 31 patients were identified (median age 70 years). Mean tumour size was 6x4cm. Chemotherapy was well tolerated with only 1 case of G4 haematological toxicity. The median number of delivered cycles was 4 (range 1-6). 23/31 (74%) had partial or complete clinical response. 11/31 (35%) proceeded to wide local excision +/- nodal dissection. The remaining responding patients received radiotherapy with radical intent +/- surgery or were deemed not fit enough for further treatment. In the NACT/surgery cohort, 4/11 patients required adjuvant radiotherapy for close or positive margins. 7/11 patients developed local relapse and 6 died of disease (1 patient was salvaged with radiotherapy). To date, 5/11 patients are alive and disease free.

Conclusions: Clinical response rate with NACT is high but surgical operability rates are low and patients are at significant risk of local relapse. Trimodality therapy incorporating radiation may be necessary if exenteration is to be avoided. Interestingly, the most significant responses to NACT were seen in younger women suggesting that HPV-related tumours may be more chemosensitive.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

A PROSPECTIVE STUDY OF LOWER LIMB LYMPHOEDEMA AND EVALUATION OF QUALITY OF LIFE AFTER VULVAR CANCER SURGERY

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Introduction: Lower limb lymphoedema (LLL) is a severe complication of vulvar cancer surgery. The aim of our study was to prospectively determine the prevalence of secondary LLL after surgical treatment for vulvar cancer using an objective. The second aim was to compare quality of life (QoL) before and 6 months after vulvar surgery.

Methods: Twenty-nine patients undergoing vulvar cancer surgery were included in our study: 17 underwent inguinofemoral lymphadenectomy (RAD) and 12 sentinel lymph node biopsy (CONS). Patients were examined before and 6 months after vulvar surgery by measuring the circumference of the lower limbs and with Multiple bioelectric impedance analysis. A control group of 27 healthy women was also measured. To evaluate QoL the European Organisation for Research and Treatment of Cancer (EORTC) quality of life questionnaires (QLQ-C30 and QLQ-CX24) were administered to patients before and 6 months after surgery.

Results: Using circumference measurement, 9 lymphoedemas (31%) were diagnosed, 3 (25 %) in the CONS and 6 (37.5 %) in the RAD group (p=0.69). After vulvar surgery patients in the RAD group reported significantly more fatigue and worsening of physical and role functioning together with worse parameters in social functioning and dyspnoea.

Conclusion: Lower radicality in inguinofemoral lymphadenectomy shows a trend towards lower morbidity and significantly improves quality of life. Detection of lymphoedema based on subjective evaluations proved to have an unsatisfactory sensitivity. Less radical surgery showed objectively better results in quality of life.

The work was supported by IGA MZ CR NT 13167-4.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

VULVAR MELANOMA PRESENTS WITH HIGH RISK PATHOLOGICAL FEATURES AND IS ASSOCIATED WITH CKIT ABNORMALITIES

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Vulvar melanoma is the second most common vulvar cancer. Unlike cutaneous melanoma where increasing awareness has led to earlier diagnosis, vulvar melanoma continues to present at late stage and with poor prognosis. To promote increasing awareness, we performed a clinicopathological and literature review. We also looked at c-KIT expression, as they have been recently recognised in mucosal melanomas, including vulvar melanomas. Our series of 33 patients fitted the expected clinical profile of older women, delayed presentation, high stage, limited response to treatment and poor prognosis. Large, often multifocal, areas of melanoma in situ were usually present. The melanoma in situ varied in the degree of melanocytic proliferation and degree of atypia. Two patients showed, as well as melanoma in situ, areas of single, separated enlarged junctional melanocytes without melanocytic hyperplasia. No patients had vulvar naevi. Three patients showed lichen sclerosus (LS) associated with melanoma in situ, although no LS was found in the areas of invasive melanoma. Prognostic predictors in our study were

(1) Breslow’s depth;

(2) absence of any of the pathological risk factors satellitosis, in transit metastasis, lymph vascular stroma invasion and dermal mitosis;

(3) removal of inguino-femoral lymph nodes;

(4) lateral margin of >1cm and

(5) strong intensity of c-KIT immunohistochemistry expression.

There have been significant improvements in understanding melanoma biology in recent years, and targeted therapy may now be an option for selected patients.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

DEVELOPMENT OF THE EUROPEAN ORGANISATION OF RESEARCH AND TREATMENT OF CANCER (EORTC) QUALITY OF LIFE QUESTIONNAIRE FOR VULVA CANCER

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Background: The EORTC questionnaire modules are designed for use in cancer clinical trials across countries and cultures. Results concerning the content validation of the new EORTC Vulva cancer module are presented.

Methods: Issues emerging from a comprehensive literature review were discussed within an expert panel of EORTC collaborators. A list of issues related to vulva cancer and its treatment were generated and vulva cancer patients, health care professionals (HCPs) and members of the EORTC Gynecologic Cancer Group (GCG) assessed the relevance and relative importance of each issue beside the breadth of coverage. Results of the relevance scores, priority ratings, and interviews with patients and HCPs formed the basis for a preliminary questionnaire for pilot-testing.

Results: 1586 papers were identified of which 157 were included in the study. An issue list consisting of 104 issues were generated and presented to 47 patients and 43 HCPs from 10 different countries representing both Southern-, Mid-, and Northern Europe including English spoken patients and HCPs. Based on the relevance and priority ratings a hypothetical domain structure was identified: Vulva sensory changes, wound healing problems, lymphoedema (groin, leg, vulva), body image, sexual and urological problems. Substantial differences between patients’ and HCPs’ relevance and priority ratings were observed and qualified discussions about the domain structure.

Conclusion: The literature review revealed a paucity of QOL data and validated assessment tools available for vulva cancer patients. The patients’ interviews and ratings proved useful as guidance of the patients’ preferences regarding a future quality of life assessment instrument.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

VIDEO PRESENTATION ON ‘LAPAROSCOPIC TRANSPOSITION OF OVARIES WITH EXTRA-PERITONEAL TUNELLING’

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The need for ovarian transposition arises in gynaecological and other pelvic cancers such as rectal cancers and sarcoma prior to radiotherapy treatment. Preservation of ovarian function prevents the long-term physical and psychological sequelae of oestrogen deficiency and importantly preserves oocytes for potential biological parenthood through surrogacy. The standard intraperitoneal approach to transposing ovaries leaves the patient with a bridge/ovarian pedicle running from the pelvic brim to the peritoneum of the anterior abdominal wall. Vascular obstruction within this bridge can result in thrombosis leading to ovarian failure. Small bowel loops can herniate through the space between the vascular bridge and the abdominal wall.

Our surgical technique involves creating an extra-peritoneal tunnel through which the ovaries are swung laterally and cephalad and then returned to the peritoneal cavity through a fenestration in the peritoneum in the mid-axillary line 8-10 cm above the anterior superior iliac supine.

Using a standard 3 or 4 port laparoscopic approach and harmonic scalpel, our technique involves the following steps:

Step-1: Bilateral salpingectomy.

Step-2: Transecting the ovarian ligament.

Step-3: Mobilisation of the ovary with its vascular pedicle above the pelvic brim.

Step-4: Creating a peritoneal tunnel.

Step-5: Swinging the ovarian pedicle through the tunnel and delivering the ovary back to the peritoneal cavity through a peritoneal fenestration.

Step-6: Suturing the ovary to the peritoneal edge.

This technique retains the ovarian vessels in the extraperitoneal space with less traction on the vascular pedicle, thereby reducing the risk of vessel thrombosis and avoiding the risk of bowel strangulation.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

DEBULKING OF RECURRENT EPITHELIAL OVARIAN CANCER (EOC) USING NEUTRAL ARGON PLASMA (PLASMAJET™)

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Background: Studies have demonstrated the efficacy of surgery for epithelial ovarian Cancer (EOC) provided optimal cytoreduction is achieved. PlasmaJet™ (PJ) is a new device designed for both laparoscopic and open surgery producing a jet of argon plasma by heating argon gas.

Discussion: Recent studies have demonstrated the efficacy of secondary debulking surgery for recurrent EOC provided optimal cytoreduction is achieved. PlasmaJet™ is a new device designed for both laparoscopic and open surgery which produces a fine jet of argon plasma by heating argon gas. Energy from argon plasma is rapidly dissipated as light, kinetic energy and thermal energy and dessicates and vaporizes soft and hard tissues allowing haemostasis and tissue cutting. The depth of penetration of the device is very superficial with minimal lateral heat spread enabling tumour ablation on visceral serosal surfaces with virtually no blood loss and without neighbouring tissue damage.

We have used this device successfully in both open and laparoscopy to debulk women with ovarian malignancy.

Description of video presentation: Video to demonstrate the use of PlasmaJet™ to achieve debulking and optimal cytoreduction for EOC.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

EFFECTIVENESS OF SPCD PLUS LMWH AS PROPHYLAXIS AGAINST VTE IN PATIENTS UNDERGOING GYNECOLOGIC ONCOLOGY SURGERY

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Clinical equipoise exists regarding the optimal prophylaxis against VTE in the surgical gynecologic oncology population.

The objective of this study was to determine if the VTE event rate is decreased in surgical gynecologic oncology patients with the addition of Sequential Pneumatic Compression Devices (SPCD) to pharmacologic prophylaxis (LDUH or LMWH).

Study Methods: A chart review of patients treated surgically by the division of gynecologic oncology at Western University was undertaken creating two cohorts: control cohort - patients receiving pharmacologic prophylaxis alone (standard prior to July 2008); and intervention cohort - patients receiving pharmacologic prophylaxis plus SPCDs (standard after August 2008). The DAD (discharge abstracting database) was searched to determine the VTE event rate during post-operative hospitalization. Our pharmacy database was searched to determine patients treated therapeutically with Heparin or LMWH for VTE. Descriptive statistics were used to compare cohorts.

Result: From January 2005 until July 2008, 1250 patients were prophylaxed prior to surgery with LDUH or LMWH. From August 2008 to present, 891 patients were prophylaxed with LMWH and SPCD. Groups were similarly distributed in terms of age and surgical length, but differed on surgical type (laparotomy versus laparoscopy) and diagnosis. The VTE event rate in the control cohort was 1.4% compared to an event rate of 2.9% in the intervention cohort.

Conclusion: The introduction of SPCD did not have the intended consequence of decreasing the VTE event rate. Further research is required to determine if SPCD in addition to pharmacologic prophylaxis decreases the VTE event rate in patients treated surgically by gynecologic oncologists.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

A NOVEL APPROACH TO MINIMALLY INVASIVE RETROPERITONEAL LYMPH NODE DISSECTION - OVERCOMING ANATOMICAL LIMITATIONS

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Goals: To introduce a simple and safe method of accessing retroperitoneal lymph nodes in patients undergoing minimally invasive surgery that require pelvic and/or para-aortic lymph node sampling for staging procedures. Demonstrate surgical technique in an instructional video to confer the practically of adopting the procedure to patient care.

Methods: During the study period, all patients undergoing robotic or laparoscopic assisted staging procedures were evaluated for need for additional mobilization of peritoneum. After placement in maximal Trendelenberg position, the small bowel was deflected along the mesentery superior to the pelvic brim. In those patients whose mesentery was determined to be “short”; in that initial maneuvers were not sufficient to stabilize the small bowel, novel technique was performed. Linear dissection of the peritoneal edge overlying the aorta with monopolar current was performed and peritoneal attachments dissected to mobilize the peritoneal edge. Afterwards, a figure of eight Endostitch™ technique with performed and the peritoneal edge deflected laterally by placement of the stitch in an extracorporeal fashion.

Results: The peritoneal dissection techniques enabled us to stabilize the small bowel and perform para-aortic and pelvic lymph node dissection in patients whose habitus and/or co-morbidities may have prevented successful staging during minimally invasive approach.

Conclusion: Dissection of the peritoneal edge along the aorta and/or pelvic vessels and subsequent fixation to an extracorporeal location provides an alternative to additional port sites and is associated with limited intra-operative morbidity.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

IS TOPICAL IMIQUIMOD THE FIRST LINE TREATMENT FOR USUAL TYPE VULVAR INTRAEPITHELIAL NEOPLASIA? A META-ANALYSIS

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Object: VIN is a relatively rare condition but its annual incidence has increased during past two decades. Recurrence rate is high and important is the potential disfigurement of the vulvoperineal unit. We conducted a meta-analysis on the published literature on the treatment of usual type vulvar intraepithelial neoplasia (uVIN) with imiquimod cream in order to quantify efficacy.

Material and methods: A search was carried out up to 2008 using: PubMed, EMBASE and the Cochrane Library. The main meta-analysis was carried out on 2 retrospective reviews, 4 prospective observation studies, 1 phase II study and 2 placebo randomized controlled trials for a total number of 66 patients.

Results: Partial response varied from 8% to 50% and complete response from 23% to 81%. Nine patients during the study follow-up presented a relapse after complete response. In 2% of the patients there was a progression to squamous cell carcinoma.

Conclusion: Data from the present metanalysis indicate that imiquimod is an active treatment for uVIN, as the overall observed response rate was 50%. Agreement with literature we feel that primary treatment of uVIN in young patients should be with Imiquimod cream. The results indicate that uVIN patients can be split into two groups, good responders and non-responders. It was not possible identify factors which can predict treatment response in advance. Response to treatment, conversely, can be viewed as a “biological” test to distinguish those lesions which are expression of viral infection from those which are true pre-cancer and need to be surgically removed.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

SENTINEL LYMPH NODE MAPPING CAN REPLACE INGUINAL LYMPHADENECTOMY IN THE SURGICAL MANAGEMENT OF CANCER OF THE VULVA

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Objective: To determine the detection rate, sensitivity and negative predictive value (NPV) of sentinel lymph node (SLN) mapping in patients with clinical early vulvar cancer.

Methods: We reviewed the medical records of 108 patients who had radical vulvar surgery with SLN mapping using lymphazurin and/or Technetium (TC99) from January 2001 to October 2011. On final pathology, the SLNs were ultra staged (6 levels with H&E + one level with immunohistochemistry).

Results: Lymphazurin alone was used in 14 patients, TC99 alone in 47 and both techniques combined in 47. At least one SLN was identified in 99.1% of cases (107/108). For the 46 patients with a “midline” tumour, bilateral SLN detection was evidenced in 73.9% and in one patient no SLN was identified. For the 62 who had a “lateral” tumour, an ipsilateral SLN was identified in 100%. Complete inguinal lymphadenectomy was performed after SLN excision in 90.7% of the patients. On final pathology, 25 patients (23.1%) had node metastasis. Of those, 7 (20.8%) were micrometastasis or isolated cancer cells. There was no false negative SLN. The sensitivity for the SLN to detect a lymph node metastasis was therefore 100% (25/25) and the NPV was also 100% (107/107).

Conclusion: In patients with vulvar cancer, SLN mapping is very reliable to detect inguinal node metastasis, specifically micro metastasis. These results, combined with others, confirm that, in the surgical management of vulvar cancer, it is safe to avoid complete inguinal lymphadenectomy when a SLN is detected and is negative.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

TRENDS IN WOUND COMPLICATIONS ASSOCIATED WITH GROIN NODE DISSECTION IN VULVAR CARCINOMA

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Background: Vulvar carcinoma is treated by partial radical vulvectomy with unilateral or bilateral inguinal-femoral lymphadenectomy (IFL). Associated wound breakdown has been reported from 14-34%. Studies have been undertaken to determine if patients could benefit from a less extensive procedure, such as sentinel lymph node mapping, decreasing acute morbidity without a loss of efficacy.

Methods: We undertook a retrospective review of acute wound morbidity associated with IFL at our institutions from 1/1/1989-12/30/2009. Individual subjects were identified and stratified by IFL. For timeline analysis, procedures were assigned to 7 year groups, Gp 1 1989-95, Gp 2 1996-2002, and Gp 3 2003-09. Our primary and secondary outcome was acute and chronic wound complications. The null hypothesis is that wound morbidity has not declined over time.

Results: Records of 421 patients including 679 groins were reviewed. (Gp1=223, Gp2= 284, Gp3=171). The average age was 63 yrs, and average weight 77.7 Kg. Incisional length decreased, (Gp1=7.4 cm, Gp2=6.9 cm, Gp3=7.2 cm) (p = 0.0498). Node count per groin remained stable, (Gp1=7.6, Gp2=7.5, Gp3=7.1) (p=0.2829). Wound breakdown was unchanged, (Gp1=10.3%, Gp2=10.2%, Gp3=9.9%) (p=0.51). The incidence of cellulitis improved, though not statistically significant (Gp1=16.1%, Gp2=16.9%, Gp3=12.8%) (p=0.43). Lymphocyst formation decreased (Gp1=13.4%, Gp2=9.5%, Gp3=6.4%) (p=0.0002) and an improvement in lymphedema was noted (Gp1=13.9%, Gp2=7.3%, Gp3=3.5%) (0.00075).

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Conclusions: Our data demonstrates that with and without stratification over time, IFL is associated with lower acute operative morbidity than previously reported. Innovative procedures intended to decrease operative morbidities need to be compared to current, not historical, experiences.
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CHYLOUS ASCITES: ANALYSIS OF 24 PATIENTS


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Introduction: Postoperative chylous ascites results from operative trauma to cisterna chyli or lymphatic vessels. In this study, patients who underwent surgery for gynecologic malignancy and had postoperative chylous ascites were evaluated retrospectively.

Material Method: We reviewed 1514 patients who had staging surgery for gynecologic malignancy at our institution from January 2003 to February 2012. Chylous diet and total parenteral nutrition (TPN) were the treatment modalities that were used initially in the conservative management of the patients. When there was no response to chylous diet TPN was started. Surgery was performed, when there was no response to TPN.

Results: Twenty-four patients had postoperative chylous ascites. Nine patients took chylous diet and 15 patients took TPN as the initial treatment. Totally seven (29%) patients required surgical correction, since 17 (71%) responded to conservative treatment. Surgery was required in only one of nine patient who were treated with chylous diet first, since surgery was performed in six of 15 patients who took TPN initially (p=0.132). In the TPN group, time from staging surgery to the diagnosis of chylous ascites was significantly longer in the group who required surgery compared with the group who did not (p:0.037). In addition this time wasn’t statistically different from the patients’ in the diet group who didn’t require surgery.

Discussion: Surgery is a second-line treatment option for postoperative chylous ascites since conservative management is highly effective. It may be logical to treat chylous ascites with diet rather than TPN initially in case the symptoms occur later.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

TRENDS IN INCIDENCE AND SURVIVAL IN PATIENTS WITH VULVAR SQUAMOUS CELL CARCINOMA IN THE NETHERLANDS

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Background and aims: The last two decades, treatment of patients with squamous cell carcinoma (SCC) of the vulva has changed from an extremely radical approach (en bloc surgery) towards limited surgery with the aim to decrease morbidity without compromising prognosis. The aim of this study was to describe trends in incidence and survival in patients with vulvar SCC in the Netherlands.

Methods: All patients with SCC diagnosed between 1989 and 2009 were selected from the population-based Cancer Registry held by the Comprehensive Cancer Centre, the Netherlands. Trends in age-adjusted incidence rates (WSR) were evaluated by calculating the estimated annual percentage change (EAPC). Jointpoint regression analysis was used to detect changes in trends. Five-year relative survival rates were calculated for two different time periods (1989-1999 and 2000-2009).

Results: A total number of 4348 patients were diagnosed with vulvar SCC between 1989 and 2009. Initially incidence rates decreased slightly with an EAPC of -0.3% (95% confidence interval (CI): -1.5-0.9%), while incidence rates increased significantly with an EAPC of 5.3% (95% CI:2.0-8.6%) after 2002. Five-year relative survival rates did not differ between the two time periods (68.0% versus 68.4%).

Conclusions: The incidence rate of vulvar SCC increased from 2002 onwards. Unless introduction of less radical surgery there are no differences in five-year survival rates.
Brief Communications on Breast, Surgical Techniques, Symptoms, and Vulva/vaginal Cancer

SECONDARY SENTINEL NODE BIOPSY AFTER PREVIOUS EXCISION OF THE PRIMARY TUMOR IN SQUAMOUS CELL CARCINOMA OF THE VULVA

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Background: To reduce treatment related morbidity of radical groin dissection, the sentinel node (SLN) procedure was implemented in the surgical treatment of early stage vulvar cancer. However, feasibility and safety of the procedure after previous vulvar surgery remain unclear.

Methods: One-hundred-and-six consecutive patients with primary vulvar cancer undergoing SLN procedure at our center were analyzed. Seventy-four patients received the SLN procedure concomitant to vulvar surgery ["primary sentinel group" (PSG)], while 32 patients had vulvar surgery before secondary SLN ["secondary sentinel group" (SSG)].

Results: SLN detection was possible in all 106 patients. Three (9.4%) patients in the SSG and 30 (40.5%) in the PSG had metastatic SLN and underwent radical groin dissection. Median interval between vulva surgery and secondary sentinel was 34 days (7-98). In the SSG tumor stages were significantly earlier with smaller tumor size (median 19mm in the PSG vs. 9mm in the SSG), and lesser invasion depth (4 vs. 2mm), p< 0.001. There were no groin recurrences in the SSG and 5.4% in the PSG. No significant difference regarding disease-free survival (DFS) could be detected: 3-year-DFS in the PSG was 72.5% compared to 92.5% in the SSG (median DFS not reached, p=0.114). Adjusting for potential confounders, such as tumor stage, nodal status, tumor size and invasion depth did not alter the results with regard to DFS.

Conclusions: Our results suggest that secondary SLN procedure after previous vulvar surgery is feasible and can accurately reflect the groin status of selected patients. Ideally, prospective trials should be conducted to verify accuracy and oncologic safety.
Brief Communications on Cervical Cancer

HEMOGLOBIN LEVEL IN CERVIX CANCER: A SURROGATE FOR AN INFILTRATIVE PHENOTYPE

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Background: Hemoglobin (Hb) is a well-known prognostic factor in cervix cancer. We hypothesized that a low Hb level, before or during radiotherapy (RT), is a surrogate for an infiltrative disease leading to uterine corpus invasion and nodal metastases.

Methods: This is a review of prospectively collected data set where locally advanced cervix cancer patients were treated by chemoradiotherapy. Eligible patients had a pre-treatment PET-Scan and MRI. Follow-up data were collected in our Gynaecology Database.

Results: Between October 1998 and December 2008, 263 patients were eligible. Median follow-up was 38.7 months. Ninety-six patients (36.5%) had both uterine corpus invasion (C+) and PET positive nodes (N+). The 3-y DFS (40.1% vs 76.1%) and OS (59.7% vs 83.1%) were lower in that group (C+N+) compared to the remaining patients (not C+N+) (p< 0.001 for DFS and OS). Patients with C+N+ disease were more likely to have a pre-treatment Hb level or Hb nadir during RT of less than 120 g/L, and a low Hb level, before and during RT, was significantly indicative of a higher recurrence rate (p=0.047 and p=0.002, respectively) and lower overall survival (p=0.004 and p< 0.001, respectively). When dividing the patients into the two prognostic groups (C+N+ and not C+N+), the positive correlation between Hb level and recurrence disappears.

Conclusions: The presence of C+N+ is associated with lower Hb levels and worst prognosis. As C+N+ state is related to tumour development and growth, it is unlikely that the correction of anemia at the time of treatment will improve survival.
Brief Communications on Cervical Cancer

CHANGES IN CYTOLOGICAL SAMPLING GUIDELINES IN YOUNGER WOMEN: A CAUSE FOR CONCERN?

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South Warwickshire has a female population of 134956, and we perform 22000 cytological analyses a year, with 2200 in the 25-29 year old age group. We analysed all the cytology in women aged 25-29 during the period 1998-2010. In addition we looked at the colposcopic findings in this period and the incidence of cervical cancer in younger women for South Warwickshire and for the UK.

There is no substantive evidence of a rise in the incidence of cervical cancer in younger women from these data although the national trend is more worrying, and requires careful scrutiny. A combination of earlier screening practice and a more interventional approach may have resulted in unnecessary cervical surgery in young women in the past, although the number of high grade cytology detected at first screening has not changed. The fall in those classified as 'moderate' is offset by an increase in those classed as 'severe' in this age group. The underlying concern is that a severely dyskaryotic sample in a young women may present as invasive at first sampling. However, there is no evidence to date that this is the case.
Brief Communications on Cervical Cancer

SOCIODEMOGRAPHIC FEATURES OF A SCREENED POPULATION IN ONTARIO, CANADA

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Introduction: A cervical cytology based screening program is effective if there is regular screening of the ‘at risk’ population and close follow-up of those labeled abnormal.

Objective: To determine the sociodemographic factors associated with cervical cancer screening and follow-up of abnormal results.

Design: This is a population cohort study.

Setting: Ontario from 2008-2010.

Participants: Women between 20-69 year old who were eligible for a Pap test.

Interventions: Using administrative data we evaluated the rates of cervical cancer screening and follow-up of high grade abnormal and cancer Pap tests Main outcome measures: Assessment of variation in Pap test performance was associated with age, area level income and health region. M. screening and follow-up.

Results: 3.8 million women were eligible for screening of whom 73% had a Pap smear in the prior 3 years. These rates varied by age, income and region. Women residing in the lowest income neighborhoods were less likely to be screened. Only 59.5% of those with an high grade abnormality (ie., atypical squamous cells suspicious for high grade abnormality, high grade squamous epithelial lesions, squamous cell cancer, atypical glandular cells, adenocarcinoma in situ, adenocarcinoma) had a colposcopy within 3 months and this varied by age, income and region.

Conclusions: Despite universal health coverage, cervical cancer screening rates are suboptimal with low income women at greatest risk (I assume you mean greatest risk of not being screened; these data do not speak to their risk of cervical cancer). Follow-up among women with high grade abnormal tests is less than ideal. Novel models of cervical cancer screening including recruitment strategies and follow-up of screen +ve cases requiring diagnostic or therapeutic interventions are needed to address these inadequacies.
**Brief Communications on Cervical Cancer**

**RETROSPECTIVE ANALYSIS OF ABDOMINAL RADICAL TRACHELECTOMY IN OUR 140 CASES**


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**Objective:** Fertility sparing surgery for cervical cancer is in demand due to the increase of cervical cancer in young women. Abdominal radical trachelectomy (RT) is one of the alternative promising surgical option. We retrospectively analysed planned 156 abdominal radical trachelectomy of our institution from 2002 September through 2011 December.

**Methods:** Surgical complication, oncological prognosis, and obstetrical outcome were estimated.

**Results:** The median age of the patients was 33 (23-44) years. The majority of the lesions were stage Ia (17.9%) or Ib1 (82.1%). In histology, 82% (116/140) were squamous and 17% (24/140) were adenocarcinomas. The median follow-up was 30.5 (3-104) months. Ten % of patients planned RT were abandoned and converted to hysterectomy due to positive lymph nodes or positive margins of the removed cervix by frozen section in the original operation. Furthermore, additional 9% of patients who underwent RT received adjuvant chemotherapy and/or radiation for those reasons. There were some post operative complications; cervical stenosis, amenorrhea and lymphocele. In the obstetrical outcome, 15 babies were delivered by Caesarean section and 5 cases were pregnant. Seventeen of 24 patients conceived with artificial reproductive technology. Nine babies were delivered after 32 weeks.

**Conclusion:** RT seems to be an oncologically safe procedure in well-selected patients with early-stage diseases. Obstetrical outcomes post RT was tolerable. However, the patients need to be fully informed about perioperative and late complications especially for the risk of premature delivery. Collaboration with gynecologic oncologists, perinatologists, ART specialists and professional nurses were also critical issues for establishing this procedure.
Brief Communications on Cervical Cancer

PRIMARY SURGERY AND TAILORED ADJUVANT THERAPY FOR STAGE 1B2 CERVICAL CANCER

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Aim: To determine the long-term survival and morbidity of patients treated by primary surgery and tailored adjuvant therapy for stage 1B2 cervical cancer.

Materials and methods: Ninety three patients, were treated in this manner at The Royal Hospital for Women in Sydney from 1989 - 2009. The mean age of the patients was 46 years. Histologic type was squamous cell in 65 cases (69.8%), adenocarcinoma in 14 (15.1%), and adenosquamous in 14 (15.1%). Vascular space invasion was present in 65 cases (69.8%), outer third stromal invasion in 73 cases (78.5%), and microscopic parametrial invasion in 15 cases (16.1%). Positive lymph nodes were present in 42 cases (45.2%). Adjuvant radiation was given to 74 patients (79.6%) - this was small pelvic field in 29 patients (31.2%), whole pelvic radiation in 17 (18.3%) and extended field (pelvic and paraaortic) in 28 (30.1%). Thirty one patients (33.3%) received concurrent chemotherapy.

Results: The median follow-up was 96 months, with a range of 6 to 283 months. The actuarial 5-year survival was 81%; it was 85% for patients with negative nodes and 76% for patients with positive nodes (p = 0.045). Long term surgical morbidity occurred in 10 patients (10.8%) (mainly lymphoedema), while long term radiation toxicity occurred in 9 patients (9.7%), three of whom had grade 3 radiation toxicity. Two necessitated surgery for small bowel obstruction and one a colostomy for large bowel obstruction.

Conclusion: Primary surgery and tailored adjuvant therapy give excellent results in patients with stage 1B2 cervical cancer, with acceptably low morbidity.
Brief Communications on Cervical Cancer

THE VALUE OF HIGH-RISK HUMAN PAPILLOMAVIRUS (HR-HPV) TEST IN THE FOLLOW-UP OF HIGH-GRADE CERVICAL LESIONS

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Objectives: To validate the effectiveness of HR-HPV test as the predictor of recurrence in high-grade cervical lesions.

Methods: Retrospective study. Between November 2003 and December 201, 217 patients who underwent conization cervical intraepithelial neoplasia (CIN) grade II, III were enrolled in this study. The patients were followed up every three to six months with cervicovaginal smears and HR-HPV test. The colposcopy and biopsy were performed for the suspected patients of recurrence.

Results: Of the 217 patients, the resection margin was involved in 70 patients (32.3%), and 25 patients (11.5%) showed positive HR-HPV test at 3 months postoperatively. There were 11 recurrences (5.1%; 7 true recurrences, 4 persistent lesions). Of the patients with positive resection margin, 9 patients were considered as recurrence (12.9%; 5 true recurrences, 4 persistent lesions). The positive predictive value (PPV) of resection margin was 12.9% and the negative predictive value (NPV) was 98.6%. Among the 25 patients with positive HR-HPV test at post-operation, there were 9 recurrent diseases (PPV=36.0%). In the subgroup of 70 patients with positive resection margin, 11 patients revealed positive post-treatment HR-HPV test. And, among the 11 patients, 7 patients were confirmed as having recurrent disease (PPV=63.6%, NPV=96.6%).

Conclusions: HR-HPV test is useful in the follow-up of the patients who treated for high-grade CIN, and it is more important in the patients with positive resection margins. When the HR-HPV test is negative in the patient with positive resection margin, there is little chance of recurrence.
Brief Communications on Cervical Cancer

CLINICAL IMPLICATIONS OF HUMAN PAPILLOMAVIRUS GENOTYPE IN CERVICAL ADENO-ADENOSQUAMOUS CARCINOMA

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Purpose: Our aims were to evaluate the genotype distribution of human papillomavirus (HPV) and the correlation between HPV parameters and clinicopathological/treatment variables with prognosis in cervical adeno-adenosquamous carcinoma (AD/ASC).

Patients and methods: Consecutive patients who received primary treatment for cervical AD/ASC International Federation of Gynecology and Obstetrics (FIGO) stage I-IV between 1993 and 2008 were retrospectively reviewed. Prognostic models were constructed and followed by internal validation with bootstrap resampling.

Results: A total of 456 AD/ASC patients were eligible for HPV genotyping, while 452 were eligible for survival analysis. HPV18 was detected in 51.5% and HPV16 in 36.2% of the samples. Age >50 years old, FIGO stage III-IV and HPV16-negativity were significantly related to cancer relapse, and age >50, FIGO stage III-IV, HPV16-negativity and HPV58-positivity were significant predictors for cancer-specific survival (CSS) by multivariate analyses. HPV16-positivity was significantly associated with good prognosis in those receiving primary radiotherapy or concurrent chemoradiation (RT/CCRT) (CSS: hazard ratio [HR] 0.41, 95% confidence interval [CI] 0.21-0.78). Patients with FIGO stage I-II and HPV16-negative AD/ASC treated with primary radical surgery had significantly better CSS (P < .0001) than those treated with RT/CCRT.

Conclusion: Age >50, FIGO stage III-IV, and HPV16-negativity were significant poor prognostic factors in cervical AD/ASC. Patients with HPV16-positive stage I-II AD/ASC can be treated with either primary radical surgery or RT/CCRT, while HPV16-negative tumor might better be treated with primary surgery (e.g. pelvic exenteration for stage IVA). Those with unresectable tumor (stage IIIB) should undergo CCRT in combination with novel drugs under clinical trials.
Brief Communications on Cervical Cancer

INTENSITY-MODULATED ARC THERAPY (IMRT-RA) WITH THE USE OF FDG-PET/CT GUIDED FOR RADIOTHERAPY CERVICAL CANcer

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Purpose: To evaluate the role of FDG-PET/CT guided for radiotherapy treatment planning based on volumetric intensity modulated arc delivery.

Materials and methods: From June 2010 to December 2011, 42 patients (pts) were treated for definitive cervical cancer with IMRT-RA.

All pts received concomitant chemotherapy (agents: CDDP or CDDP plus Paxlitaxel).

CT scan was integrated either with CT/FDG-PET and MRI for gross tumour volume (GTV) delineation.

Simultaneous integrated boost (SIB) technique was employed: 45-50.4 Gy (1.8 Gy/fraction) was prescribed to the T, N0 pelvic and/or para-aortic lymph nodes and 55 Gy (2.2 Gy/fraction) to the positive lymph nodes.

For all pts the radiation treatment schedule included also a boost of 25-30 Gy to be delivered with high or pulsed dose rate brachytherapy (HDR or PDR).

Results: The FDG-PET/CT leads to a better volume definition and has the potential of showing lymph-nodes metastasis and T-tumour area. Planning target volume (PTV) was always covered by 95-107% of the prescribed dose. The mean D50% for the bladder, rectum and small bowel were 31.9 Gy, 39.8 Gy and 12.35 Gy, respectively.

Conclusions: Results from DVHs analysis showed an excellent reduction in organ at risk exposure maintaining high target coverage and conformality.

With FDG-PET/CT it was possible to definite better GTV, therefore to reduce significantly the dose of organs at risk and open the space for escalation dose regimens.
Brief Communications on Cervical Cancer

CLINICAL Efficacy of Neoadjuvant Chemotherapy IN STAGE IIB Cervical Cancer

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Objective: The purpose of this study was to compare the overall survival between neoadjuvant chemotherapy followed by radical hysterectomy (NACT+RS) and concurrent chemoradiotherapy (CCRT) or radiotherapy in patients with FIGO stage IIB cervical cancer.

Methods: We retrospectively analyzed 192 patients with stage IIB cervical cancer who had undergone NACT+RS (n=103) or CCRT (n=89) at the Catholic university Hospital between 1998 and 2009. All risk factors that may have affected the overall survival (OS) and disease-free survival (DFS) and the prognostic factors and down-staging rate of NACT were assessed.

Results: In total, 192 patients were included. Clinical characteristics were not significantly different except age between the groups. Age of NACT+RS group is lower than CCRT group. The 5-year OS of the NACT+RS and CCRT groups were 63.5% and 75.8%, respectively (P=0.016), whereas the 5-year DFS were 62.3% and 77.3%, respectively (P=0.033). The NACT+RS group showed no statistical differences in DFS and OS than CCRT (DFS: hazard ratio =1.207, P=0.521; OS: hazard ratio = 1.339,P=0.327) groups, while adjusting for age. The response rate in NACT+RS group was 39.8%. Postoperative adjuvant therapy in NACT+RS group was 91.3%.

Conclusions: The results of our study suggest that NACT+RS does not improve the OS and DFS in patients with stage IIB cervical cancer compared with CCRT. In NACT+RS group, postoperative adjuvant therapy was more common. Therefore, CCRT is considered the primary treatment than NACT+RS in patients with stage IIB cervical cancer.
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GALECTIN-1 EXPRESSION IS ASSOCIATED WITH TUMOR INVASION AND METASTASIS IN EARLY CERVICAL CANCER


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Objective: Galectin-1 (Gal-1) is a 14-kDa laminin-binding lectin involved in important biologic mechanisms of tumors, including neoplastic transformation, cell survival, angiogenesis, cell proliferation, and metastasis. In this study, we investigated the role of Gal-1 in cell survival and metastasis in cervical cancer.

Methods: The expression of Gal-1 was determined in 73 formalin-fixed, paraffin-embedded cervical cancer tissues using an immunohistochemical method and compared with clinicopathological risk factors for recurrence after surgery. To evaluate the role of Gal-1 in cell proliferation and invasion, we performed proliferation and invasion assays with Gal-1 siRNA using cervical cancer cell lines, including HeLa and SiHa cells.

Results: Immunohistochemical analysis revealed that Gal-1 expression was found in the majority of peritumoral stroma samples (72/73; 98.6%) and occasionally on the tumor cells proper (22/73; 30.1%). Gal-1 expression was significantly correlated with the depth of invasion in the cervix ($P=0.015$) and lymph node (LN) metastasis ($P=0.049$). Down-regulation of Gal-1 using siRNA resulted in the inhibition of cell growth and proliferation of HeLa and SiHa cells. Moreover, the ability of cells to invade was significantly reduced by Gal-1 siRNA.

Conclusion: Our results revealed that high Gal-1 expression was significantly correlated with depth of invasion in cervical lesions and LN metastasis of cervical cancer, and Gal-1 may be functionally involved in cell proliferation and invasion. Therefore, Gal-1 has potential for use as a prognostic marker and therapeutic target.
Brief Communications on Cervical Cancer

DIFFUSION-WEIGHTED MR IMAGING IN PREDICTING AND MONITORING THE EARLY RESPONSE OF UTERINE CERVICAL CANCER TO CONCURRENT CHEMORADIATION

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Objective: To investigate the feasibility of DWI in predicting and monitoring the early response of uterine cervical cancer to concurrent chemoradiation and choose the optimal time that can detect the treatment response as early as possible.

Materials and methods: Thirty-three patients with uterine cervical cancer received conventional MRI and DWI examinations prior to therapy and at three days, seven days, fourteen days, one month and two months after the therapy initiated. They all received concurrent chemoradiation within a week after MRI examination. The longest tumor diameters and ADC values were measured.

Results: Pretreatment ADC value of CR was significantly lower than that of PR ($p=0.007$). The percentage ADC change of CR at either follow up time was greater than that of PR, and the differences were significant at the time of fourteen days ($p=0.007$) and one month ($p=0.001$). There was a significant correlation between the percentage size reduction of tumor after two months of treatment and pretreatment ADC value ($p=0.045$). At the time of three days, seven days, fourteen days and one month after the therapy initiated, there was positive correlation between the percentage ADC change and the percentage size reduction of tumor after two months of therapy ($p=0.014$, $p=0.026$, $p=0.000$, $p=0.001$).

Conclusion: It is feasible to use DWI to predict and monitor the treatment response of uterine cervical cancer to concurrent chemoradiation, and the optimal time for monitoring the early treatment response is the day of fourteen after the therapy initiated.
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RESULTS OF LAPAROSCOPIC RADICAL HYSTERECTOMY AFTER PREOPERATIVE BRACHYTHERAPY FOR STAGE IB1 CERVICAL CANCER IN A LARGE STUDY OF 162 CASES

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Background: The aim of this study was to report the feasibility and results of laparoscopic radical hysterectomy (LRH) after initial uterovaginal brachytherapy (BT) for stage IB1 cervical cancer.

Methods: We retrospectively reviewed in two Comprehensive Cancer Centers patients who had undergone initial BT followed 6 to 8 weeks later by LRH and lymph node dissection.

Results: Between 2003 and 2010, 162 patients had undergone LRH. The procedure was feasible using this approach in 160 (98.8%) cases. Eight pre-operative complications had occurred. Nineteen patients had nodal involvement. Peri- or post-operative ureteral morbidity had occurred in 10 (6%) patients. Twenty-four (15%) patients had experienced post-operative dysuria. Histologically, only 9 patients had residual cervical disease ≥ 5 mm and only 1 patient had parametrial lymphovascular space involvement (associated with nodal spread). No patient had vaginal disease or involved surgical margins. After a median follow-up of 39 months (range, 3-118), 9 patients had relapsed. Five-year overall survival was 95% (88.2%-97.9%).

Conclusions: Radical hysterectomy using a laparoscopic approach is feasible and reproducible after initial BT for stage IB1 cervical cancer and is associated with excellent survival. Morbidity is very close to that reported in patients treated using upfront surgery. In this large series, the morbidity associated with parametrial dissection and the fact that parametrial spread was observed in only 0.6% of the patients suggest that a simple extrafascial hysterectomy is probably sufficient in this context (the rate of urinary tract morbidity would then be reduced).
Brief Communications on Cervical Cancer

**LAPAROSCOPIC VERSUS OPEN RADICAL HYSTERECTOMY IN PATIENTS WITH STAGE IB2 AND IIA2 CERVICAL CANCER**


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**Objectives:** To compare survival and surgical outcomes of laparoscopic (LRH) and open radical hysterectomy (ORH) in patients with stage IB2 and IIA2 cervical cancer.

**Methods:** A retrospective analysis was performed on 303 patients with stage IB2 and IIA2 cervical cancer who underwent LRH (n=115) or ORH (n=188).

**Results:** Two patients (1.7%) in the LRH group required conversion to laparotomy. After surgery, 75 patients (65.2%) in the LRH group and 127 patients (67.6%) in the ORH group received adjuvant therapy (P=0.676). After a median follow-up time of 30 months (range, 3-142 months), 5-year disease-free survival was 78% in the LRH group and 77% in the ORH group (P=0.718), and 5-year overall survival was 83% in both groups (P=0.746). There were no differences in pattern of recurrence (P=0.225) and median time to recurrence (12 vs. 13 months; P=0.240). There was also no difference with respect to operating time, perioperative change in hemoglobin level, and need for transfusion. However, in the LRH group, estimated blood loss (P=0.003) was significantly lower, time to recovery of bowel movement (P<0.001) and length of postoperative hospital stay (P<0.001) were significantly shorter, and postoperative complications were significantly less frequent (P=0.036).

**Conclusions:** LRH has similar therapeutic efficacy to ORH. However, LRH has more favorable surgical outcomes including less estimated blood loss, faster recovery of bowel movement, shorter hospital stay, and fewer postoperative complications. Therefore, LRH is not only a reasonable alternative to ORH but also the preferred surgical procedure for experienced laparoscopic oncologic surgeons.
Brief Communications on Cervical Cancer

SIMPLE VAGINAL TRACHELECTOMY AND LAPAROSCOPIC LYMPH NODE EVALUATION IN PATIENTS WITH LOW RISK EARLY-STAGE CERVICAL CANCER

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Objective: Evaluate the feasibility of simple trachelectomy and node assessment in patients with low-risk cervical cancer (< 2cm).

Study methods: From May 2007 to December 2011, 13 women with low-risk small volume cervical cancer underwent a simple vaginal trachelectomy preceeded by laparoscopic sentinel node mapping +/- pelvic node dissection. Data was collected prospectively in a computerized data base. Descriptive statistics and Kaplan-Meyer estimate were used for analysis.

Results: Patients’ median age was 28 and 11/13 were nulliparous. Five had a cone, 5 a LEEP, 2 had biopsies and one polyp excision. Three patients had stage IA1 with LVSI, 5 IA2 and 5 IB1. Eight (61.5%) had squamous lesions, 5 had adenocarcinoma. LVSI was present in 3 cases, suspicious in 2 and absent in 8. There were two surgical complications: a trocar site hematoma and a vaginal laceration. The median OR time was 149 min (range: 120-180) and median blood loss was 73 cc (range: 50-150). On final pathology, lymph nodes were negative in all patients. Eleven patients (85%) had either no residual disease in the trachelectomy specimen (4) or residual dysplasia only (7). Only 2 had residual microscopic disease. With a median follow-up of 15 months (range: 1-56), there have been no recurrences. The recurrence-free survival at 24 months is 100%. One patient conceived and delivered at 39.5 weeks.

Conclusion: Simple trachelectomy and nodes appears to be a safe alternative in well selected patients with small volume disease. Our data will need to be confirmed in larger series.
Brief Communications on Cervical Cancer

PREVALENCE AND RISK FACTORS FOR ONCOGENIC HPV INFECTION AMONG HIV INFECTED AND UNINFECTED RWANDAN WOMEN

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Background: Cervical cancer, which is caused by oncogenic HPV types, remains a major public health issue in developing. Secondary prevention through large-scale cytological screening programs have reduced cervical cancer incidence in developed countries. While barriers to implementation these programs, such as costs and lack of needed health infra-structure remain it is still important to know the prevalence of HPV induced cervical cancer risk in important populations. We assess the prevalence and risk factors for oncogenic HPV infection in HIV infected and uninfected Rwandan women.

Methods: We tested, 3008 Rwandan women for oncogenic HPV infection with a point of care test, careHPV®, which detects 15 HPV carcinogenic strains. Stepwise selection logistic regression built multivariate predictive models of oncogenic HPV infection. Odds ratios (OR) with 95% confidence intervals (95% CI) quantified the magnitude of association of oncogenic HPV infection with HIV and other potential confounders and mediators. P-values less than 0.05 were considered statistically significant.

Results: Oncogenic HPV prevalence was significantly higher in HIV infected women (31.7% vs. 9.0%, p< 0.001). In multivariate analysis of all participants, HIV infection was independently associated with oncogenic HPV infection; aOR=4.0; 95 % CI 3.1- 4.9 as well as age, and age at first pregnancy. In HIV positive women, low CD4 cell count: < 200 cells/ µL (aOR=1.9; 95 % CI 1.2 - 3.1), Age, age at first pregnancy, more lifetime sexual partners and hormonal contraceptives had significant independent associations with oncogenic HPV infection.

Conclusion: Our data showed a high prevalence of oncologic HPV infection in HIV seropositive and seronegative women. HIV infection was independently associated with greater oncogenic HPV with high magnitude of association. In HIV infected women, those with severe immunodepression as indicated by low CD4 cell count were more likely to have infection with oncogenic HPV strains.
Brief Communications on Cervical Cancer

LOCATION, LOCATION, LOCATION: IMMUNE RESPONSES IN PATIENTS WITH CIN3 RECEIVING THERAPEUTIC HPV16E7 VACCINATION

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Objective: Two recent clinical trials evaluating therapeutic HPV vaccines in women with VIN have reported complete responses in excess of 40%, over a 52-week study window. These trials demonstrate that regression of high grade intraepithelial lesions can occur in subjects with modest systemic immune responses to vaccine antigens, and that responses “accumulated” over a longer timeframe than typically used in trial design. We sought to evaluate a novel HPV16E7 vaccine in patients with CIN3.

Methods: A phase I trial is being conducted testing intradermal, intracervical, and intramuscular routes of administration of a DNA vaccine targeting HPV16E7, in subjects with HPV16+ CIN3, prior to LEEP 8 weeks post-vaccination. Clinical trial endpoints include assessment of regression of CIN, and immune response.

Results: No significant vaccine-associated toxicity has been noted. Within-subject analyses of tissue specimens from the intradermal vaccination cohort demonstrate an increase in cervical CD8+ infiltrates pre- and post-vaccination, resulting in an increased ratio of CD8:Treg cells. The density of Tbet+ infiltrates increased an average of 4.6-fold in lesional epithelium and by 7.6-fold in lesional stroma. The distribution of Tregs was greater in lesional stroma compared to epithelium at both timepoints. Accrual to this trial is ongoing, and similar analyses of tissue immune cell infiltrates will be presented.

Conclusion: Increased densities of Tbet+ cells in both the stromal and epithelial compartment of cervical mucosa suggest the generation of Type I immunity. The distribution of Tregs suggests that the stromal compartment may play a role in conditioning immune responses in persistent mucosal HPV infections.
Brief Communications on Cervical Cancer

SAFETY, ACCEPTABILITY AND FEASIBILITY OF COMMUNITY-BASED CAREHPV FOR CERVICAL CANCER PREVENTION IN RURAL THAILAND

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Objective: To assess the safety, acceptability and feasibility of field-based primary HPV testing for cervical cancer prevention program in a low-resource setting.

Methods: This pilot project involved two phases. 1) Training technicians to run specimens on the careHPV unit, and 2) Implementation of HPV testing in the field. The study team traveled to a different village each day in rural Roi-et Province, Thailand. Women were tested for presence of HPV using self-swab, followed careHPV testing. Those positive were assessed immediately by visual inspection (VIA). HPV and VIA positive women were offered cryotherapy. Safety was determined by monitoring adverse events. Exit surveys assessed acceptability and feasibility. Feasibility was also assessed by measuring the testing and triage throughputs.

Results: Overall: Technical competency was achieved in 2.5 days. Over 14 days, 431 women were screened in 14 villages. HPV prevalence was 7.3%.

Safety: no adverse events were reported.

Acceptability: 90.5% of the women reported that they would take the self-swab again, 95.5% would recommend the careHPV program to a friend, and 78.9% of the women thought a self-swab was “easy.”

Feasibility: 99.8% of eligible women agreed to be tested. The total clinic time investment for an HPV-negative woman was about 32 minutes from screening to results, and 46 minutes for an HPV-positive woman (including VIA). Project staff spent on average 5.5 hours/day on the project.

Conclusions: There is a large potential for cervical cancer screening scale-up because of the careHPV unit’s ability to test specimens rapidly and simultaneously and because only 5-6% of the women (i.e. HPV positive) would require a gynecological exam. Additionally, the program was very convenient for women: testing was community-based and women spent only 30-50 minutes total time from screening to results. Savings in training time and required gynecological exams make this approach attractive for low resource settings.
Brief Communications on Cervical Cancer

SCREENING DOES NOT PROTECT AGAINST CYTOLOGICAL HSIL IN WOMEN YOUNGER THAN 25 YEARS


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Introduction: In the era of human papillomavirus (HPV) vaccination and the use of HPV-DNA testing, discussion of Pap screening is still relevant. The objective of this study was to evaluate the impact of screening on the prevalence of cervical lesions to guide understanding of the role of cytology screening.

Methods: This analysis of diagnosis prevalence from cytological screening in an urban region of Brazil involved 2,002,472 exams in previously screened women and 217,826 exams in unscreened women. For trend analysis, we used the χ2 test modified by Cochran-Armitage; to compare groups, we used the prevalence ratio (PR) with a 95% confidence interval.

Results: The PR of screened versus unscreened women was not significant for high-grade squamous intraepithelial lesions (HSIL) in women under age 20 years (PR = 0.97, 0.83-1.13) or ages 20-24 years (PR = 0.99, 0.86-1.14). In women ages 25-29, PR was 0.63 (0.52-0.76), decreasing up to ages 45-49 years to a PR of 0.19 (0.13-0.26). For low-grade squamous intraepithelial lesions (LSIL), the PR decreased significantly in women under age 20 (PR 0.89, 0.83-0.96) and ages 20-24 (PR 0.76, 0.70-0.82); for the diagnosis of squamous cell carcinoma, PR decreased significantly after ages 30-34 (PR 0.19; 0.04-0.87).

Conclusion: Screening for women under age 25 does not protect against cytological HSIL or invasive lesions in this age group. The prevalence of LSIL reduced a little but this finding is not relevant to set standards or recommendations.
Brief Communications on Ovarian Cancer

RESPONSE TO SECOND LINE CHEMOTHERAPY IN EPITHELIAL OVARIAN CANCER PATIENTS TREATED ON NEOADJUVANT CHEMOTHERAPY PROTOCOL

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Objectives: Response to second line chemotherapy at recurrence after completion of neoadjuvant chemotherapy has not been studied previously. We analyzed response to second line treatment stratified by primary treatment approaches.

Method: Epithelial ovarian cancer patients with first diagnosed progression were retrospectively reviewed from 2007-9. Patients' demographics, primary treatment received and response to second line therapy were abstracted from electronic medical records. Chi Square statistics were used for categorical variables. Logistic regression model was used to predict response to second line therapy using predictor variables: age, residual status, initial treatment and use of intraperitoneal (IP) chemotherapy. All p values less than 0.05 were considered to be statistical significant.

Results: 100 patients with first recurrence were reviewed. Median age was 61.7 yo. The majority had stage 3/4 disease with 70% having serous histology. Twenty two patients were treated with adjuvant IP chemotherapy. Optimal residual disease was present in 50 patients. Median follow up was 28.2 months. The median progression free survival (PFS) was 16 months. Response to second line chemotherapy was observed in 41 patients (41%). Use of neoadjuvant chemotherapy significantly increases the risk of non-response to second line therapy (OR 3.42 95% CI 1.25-9.36 p=0.02). Adjuvant IP chemotherapy significantly decrease the risk of non-response to salvage therapy (OR 0.25 95% CI 0.08-0.81 p=0.02).

Conclusion: Response to second line therapy can be significantly influenced by primary treatment administered. This should be factored into future trial designs examining the effectiveness of salvage therapy for recurrent epithelial ovarian cancer.
Brief Communications on Ovarian Cancer

PROTYPE: A RAPID GENE-EXPRESSION-BASED PREDICTOR OF OVARIAN CARCINOMA TYPES FOR USE ON SMALL PRE-SURGICAL BIOPSIES

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Background: Ovarian carcinomas are a complex collection of five major histo-types, each associated with specific clinical, epidemiological and molecular features. Neo-adjuvant chemotherapy (NAC) prior to surgery appears to primarily benefit patients with high-grade serous cancer, the most common histo-type. However, assignment of histo-type prior to surgery is challenging as small biopsy cores are sub-optimal for pathological or immunohistochemical (IHC) assessment. We have developed an RNA-expression based histo-type predictor that requires only minute input.

Methods: 250 genes were pre-selected from ovarian cancer gene-expression data sets for discrimination of histo-types. This panel was then assayed across over 268 unique ovarian carcinomas using NanoString-GX and subjected to gynecopathological review and assessment via an immuno-marker panel.

Results: Histo-types were identified using NanoString-GX data from a minimal gene-set and total-RNA input as low as 200ng. Our centroid-based predictive classifier showed agreement between a gold standard, consensus of path-review and IHC-assessment, in 95% of cases. Correlation between whole tumour samples and needle cores was high and did not affect histo-type prediction.

Conclusions: Our Predictor of Ovarian carcinoma TYPE (PrOTYPE) performs well using small samples typical of pre-surgical biopsies. Rapid and accurate pre-surgical histo-typing could have an immediate impact on healthcare resources as NAC-treated women typically have lower post-surgical morbidity and shorter hospital stays. Validation of our classifier model in a broader spectrum of biopsy samples is ongoing.
Left panel showing receiver operator characteristics (ROC) for the PrOETYPE predictive model and right panels show typical correlation between whole tumour sections and needle cores for two samples.

[Figure 1]
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DIFFERENCES IN TUMOR IMMUNE REGULATION BETWEEN AFRICAN-AMERICAN AND CAUCASIAN OVARIAN CANCER PATIENTS

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Objectives: To determine the differences in tumor immune regulation between African-American and Caucasian ovarian cancer patients.

Methods: Demographic and clinico-pathologic characteristics, outcomes, and genomic data were obtained from The Cancer Genome Atlas. Kaplan-Meier, t-test, and logistic regression were used for statistical analyses.

Results: Of 447 patients (median age was 59 years), 22 were African-Americans and 425 were Caucasians. Stage I-II vs. III-IV disease comprised of 33 (7%) vs. 412 (92%) patients. The majority (85%) had grade 3 tumors. The median and 5-year overall survivals were 45 months and 32% with a follow-up time of 31 months (range: 0-180). There were no differences in stage, grade, and rate of optimal cytoreduction between the two groups. The 5-year overall and median survival of Caucasian patients were 34% and 45 months vs. 12% and 37 months in African-American patients (p=0.11). Sixty-nine immune factors that play roles in cancer regulation or prognosis were identified from the literature. Compared to African-American patients, Caucasians had higher expression of CD4 (1.07 vs. 0.80; p=0.004), CD80 (0.74 vs. 0.53; p=0.009), CTLA4 (0.07 vs. -0.30; p=0.003), IL18 (1.11 vs. 0.56; p=0.046), IL7R (-0.67 vs. -1.53; p=0.024), and TNF (2.30 vs. 1.78; p=0.005). The differential expression of these regulatory genes are associated with cytotoxic T-lymphocyte-associated protein 4, CD80, and tumor necrosis factor.

Conclusion: Differences in expression profiles of tumor immunoregulation between African-American and Caucasian ovarian cancer patients may provide novel strategies toward individualizing cancer care.
Brief Communications on Ovarian Cancer

EPITHELIAL OVARIAN CANCER: RATIONALE FOR CHANGING THE ONE-FITS-ALL STANDARD TREATMENT REGIMEN TO SUBTYPE-SPECIFIC TREATMENT

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Objective: Classifying epithelial ovarian cancers (EOCs) only into Type I tumors (low-grade serous, mucinous, endometrioid, clear cell), harbouring KRAS or BRAF mutations, and Type 2 tumors (high-grade serous, undifferentiated cancers, carcinosarcomas), based on genetic instability, TP53 mutations and BRCA1 loss, is artificial. This study aims to stress the need for further subclassification and subtype-specific treatment.

Materials/methods: 262 primary high risk stage I or stage II-IV EOCs, collected at the University Hospitals Leuven or within the EORTC 55971 trial, were genotyped for hot spot mutations in KRAS (COSMIC coverage >97%), BRAF (>95%), NRAS (>97%), PIK3CA (>81%), FBXW7 (>66%), AKT2, AKT3 and FOXL2, using Sequenom MassARRAY. Borderline tumors were not included.

Results: Of the 13% Type I tumors, 49% were either KRAS or PIK3CA mutated. Mucinous subtypes (8/35) harboured significantly more KRAS mutations than all other histologies combined (50% vs 4%, P< 0.001), with higher prevalence in intestinal-type (67%) than in Müllerian-type (33%) (P=0.407). PIK3CA mutations were predominantly found in clear cell carcinomas (46.2% vs 2.8%, P< 0.001) and had associated endometriosis in 67% of those cases (P=0.148). Low-grade serous tumors were more frequently KRAS or BRAF mutated than high-grade lesions (44% vs 0.6%, P< 10⁻⁵). KRAS/PIK3CA mutation didn’t correlate with PFS, OS or platinumresponse. NRAS, FBXW7, AKT2, AKT3 and FOXL2 mutation frequency was less than 1%.

Conclusions: Type I EOCs contain distinct diseases with different driver mutations. Clinical trials in these subtypes are necessary to evolve the current one-fits-all regimen to evidence-based stratification, based on molecular drivers and histotype-specific treatments.
Brief Communications on Ovarian Cancer

VALUE OF TERTIARY CYTOREDUCTIVE SURGERY (TCS) IN EPITHELIAL OVARIAN CANCER (OC): AN INTERNATIONAL MULTICENTER EVALUATION

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Background and aims: The value of surgery for recurrent OC is controversial. Aim of the present study was to evaluate the outcome of OC-patients who underwent TCS and to identify prognostic markers for complete tumor resection and survival.

Methods: A retrospective multicenter evaluation of TCS-patients treated between 1997 and 2011 in 14 centers across Europe, USA and Asia was performed.

Results: We evaluated 406 patients (median age: 55y; range:16-80). Median time from primary diagnosis to 1st-recurrence was 20 months (range: 2-380) and from 1st to 2nd-recurrence 18 months (range: 2-204). Median follow-up from TCS was 14 months (range: 0-182) and median OS 26 months (95%CI:19.62-32.38). The majority of the patients had an advanced initial FIGO stage III/IV (69%), serous histology (75.4%), peritoneal-carcinosis (51.7%) and absence of ascites (72.2%). 224 (54.1%) patients underwent a complete tumor resection. The most frequent site of tumor dissemination was the pelvis (73%). Rates of major operative morbidity and 30-days mortality were 25.9% and 3.2%, respectively. 155 (38.2%) patients received platinum at 3rd-line chemotherapy. Multivariate analysis identified platinum-resistance, tumor residuals at secondary surgery and peritoneal-carcinosis to be of prognostic significance for complete tumor resection, while tumor residuals at secondary & tertiary surgery, decreasing interval to 2nd-relapse, ascites, upper abdominal tumor involvement and non-platinum 3rd line-chemotherapy significantly affected survival.

Conclusions: In this largest known database for TCS, residual tumor retains its high impact on survival even in the tertiary setting of OC. In specialized centers high rates of total macroscopic clearance can still be obtained. Prospective analyses are warranted to define the value of TCS in EOC.
Brief Communications on Ovarian Cancer

CHEMOTHERAPY-INDUCED NEUTROPENIA AS A PROGNOSTIC MARKER AMONG WOMEN WITH ADVANCED OVARIAN, TUBAL AND PERITONEAL CARCINOMA TREATED WITH PLATINUM/TAXANE-BASED THERAPY

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Background: Body surface area dosing does not account for the complex processes of chemotherapy drug elimination. Unrecognized under-dosing may occur in >30% of patients resulting in reduced cytotoxicity. Chemotherapy-induced neutropenia (CiN) may be a surrogate marker for survival.

Purpose: To determine whether CiN is associated with overall survival (OS) in a phase III trial studying sequential doublet/triplet chemotherapy in patients with advanced disease.

Methods: This is a post-hoc analysis of data from GOG 0182 investigating neutropenic status, time to completion of therapy and survival data. Neutropenia was absolute neutrophil count < 1000/mm³. Kaplan-Meier curves were generated. Landmark analysis was performed on patients receiving all 8 cycles of prescribed therapy with intact data. The 95th percentile of completion time was assigned as the landmark point.

Results: Neutropenic status was available for 3,659 of 4,312 women enrolled. Median OS was 46.9 vs. 35.2 months in the neutropenic vs. non-neutropenic groups (p< 0.001), with an adjusted hazard ratio (aHR) of 1.33 (p< 0.001). In patients receiving all cycles, intact data was available for 2,963 women included in the landmark analysis. Median OS was 48.3 vs. 40.6 months respectively (p=0.033) with an aHR of 1.16 (p=0.083). The gemcitabine triplet was the only arm to show a statistically significant difference between groups- 48.1 vs. 36.8 months (p=0.029) with an aHR of 1.65 (p=0.034).

Conclusion: These data suggest that CiN occurrence implies a survival advantage for patients with untreated advanced disease. Prospective validation is necessary with consideration for regimens known to cause more profound neutropenia.
Brief Communications on Ovarian Cancer

SEXUALITY AND QUALITY OF LIFE OF WOMEN AFTER OVARIAN OR ENDOMETRIAL CANCER

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Background: Gynecological cancer (GC) is generally assumed to have an impact on sexuality and quality of life. Although there are several studies addressing this issue, case control studies are currently limited.

Methods: We performed a cross-sectional investigation of sexual function and activity utilizing the sexual activity questionnaire, the female sexual function index, and parts of the EORTC QLQ C30. Patients with gynecological cancer (GC) like ovarian or endometrial cancer were compared with a control group (C) of non-cancer patients. Inclusion of GC was only allowed if treatment was completed ≥12 months previously and patients were disease-free.

Results: The questionnaires were sent out to 727 women (335 x GC and 392 x C), of which 22.8% responded. Response rates in both groups were equivalent (79 pts with GC [23.6%] and 87 control subjects [22.2%]). Median age was 57 years (C) and 62 years (GC), respectively (p=0.237). 51.5% (C) and 59.5% (GC) were not sexually active, mainly owing to lack of a partner (37%) or lack of interest (21%) in controls and lack of interest (40%, p< 0.05), self-reported physical problems (31.9%, p< 0.05), and physical problems of the partner (21%, p< 0.05) in the GC group. There were significant differences between both groups in the SAQ discomfort score (p< 0.05). We did not observe significant differences in quality of life or other scores regarding sexuality.

Conclusions: About half of the women in both groups were not sexually active. However, reasons for non-activity differ. Quality of sexuality tends to be impaired in GC patients, but this seems not to influence quality of life. A shift of priority caused by substantial anxiety regarding cancer specific survival might explain our findings.
Brief Communications on Ovarian Cancer

ACCELERATING TYPE-SPECIFIC OVARIAN CARCINOMA RESEARCH: CALCULATOR FOR OVARIAN SUBTYPE PREDICTION (COSP) IS A RELIABLE HIGH-THROUGHPUT TOOL FOR CASE REVIEW

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Background: The recent recognition that ovarian carcinoma is composed of five distinct disease entities has served to increase the value of accurate histotyping. Reliable identification of histotypes is essential for the success of studies testing novel therapeutics as well as for biomarker discovery research. COSP, a nine-marker immunohistochemical panel combined with a validated prediction equation, has been shown to reliably reproduce the consensus diagnosis of two expert gynaecological pathologists. We explored if COSP could be used as a high-throughput and cost-effective pathology review mechanism in clinical trial cohorts of ovarian carcinoma.

Design: A cohort of 423 cases from the ICON7 trial was evaluated by COSP. Original diagnoses from non-expert pathologists were compared to COSP results and subsequently verified by an independent gynecopathologist.

Results: Of 423 tumors COSP was able to classify 334 cases. The remaining 89 tumors could not be predicted by COSP due to missing IHC and non-specific histotype diagnoses (e.g. mixed type). The overall concordance rate between COSP and specialized gynecopathology review was 89.3%. In cases where a non-expert diagnosis was confirmed by COSP, the gynecopathologist also agreed in 97.5% of cases.

Conclusion: COSP performs favorably in our clinical trial patient cohort as was expected from previous validation exercises. COSP has the potential to serve as a high-throughput tool in ovarian carcinoma case review, saving both expert time and valuable resources by preselecting the small number of difficult cases that truly require an expert review.
Brief Communications on Ovarian Cancer

DIAGNOSTIC ACCURACY OF PET/CT IN EARLY STAGE OVARIAN CANCER: COMPARISON BETWEEN PET/CT AND CT OR MRI


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Objective: To evaluate the diagnostic accuracy of positron emission tomography/computed tomography (PET/CT), abdomino-pelvic computed tomography (CT), and pelvic magnetic resonance imaging (MRI) for detection of early stage ovarian cancer.

Methods: Medical record of 140 women who underwent PET/CT scanning with suspected early stage ovarian cancer (stage 1-2) from July 2005 to February 2012 was retrospectively reviewed. Preoperative CT, MRI, and PET/CT findings were compared with histopathologic results obtained from the surgery. The accuracy of each modality in detection of malignancy was evaluated by computing the relevant areas under a receiver operating characteristics (ROC) curve and comparisons of the area under the curve (AUC) according to the modality (MedCalc® version 9.6.3.0, Broekstraat 52, Mariakerke, Belgium).

Results: Histopathology showed 7 cases of benign tumors, 23 cases of borderline tumors, and 110 malignant tumors. In detecting malignant lesions in the ovaries and the adnexa, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of PET/CT were higher than the corresponding values of CT or MRI. In discriminating between cases of benign/borderline and malignant, the accuracy of PET/CT(0.760) trended higher than that of CT or MRI(0.585).

[ROC curve analysis]
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<tr>
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<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV</th>
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<tr>
<td>PET/CT</td>
<td>96.4 (91.1-99.0)</td>
<td>63.8 (35.1-80.8)</td>
<td>94.7</td>
<td>63.6</td>
</tr>
<tr>
<td>CT or MRI</td>
<td>95.5 (89.9-98.5)</td>
<td>55.4 (31.9-75.4)</td>
<td>90.7</td>
<td>58.6</td>
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**Conclusion:** PET/CT is more accurate than CT or MRI in diagnosis of early stage ovarian cancer and in differentiating between cases of benign/borderline and malignant ovarian tumors.
Brief Communications on Ovarian Cancer

PLASMA MICRO-RNA PATTERN RELIABLE BIOMARKER ABLE TO DIFFERENTIATE EPITHELIAL OVARIAN CANCER (EOC) FROM BENIGN PELVIC MASS (BOM)

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Background: Postmenopausal patients diagnosed with complex BOM undergo invasive pelvic surgeries to rule out ovarian cancer. The vast majority of women operated for pelvic masses do not have ovarian cancers. Aims: Are there patterns in the pre-surgical plasma miRNA profiles distinct enough to discriminate between BOM and EOC?

Methods: Between 2004 and 2011 we investigated patterns of circulating miRNAs collected before, after surgery, during and after chemotherapy in 56 patients presenting for surgery for ovarian masses and 10 normal controls. We also collected blood at ovarian cancer relapse and tumor and benign ovary for miRNA analysis. 2-sample t-test was used for all 2-sample comparison and ANOVA followed by Tukey HSD post-hoc test to compare the mean response between subject factors of interest. All tests were 2-tailed and results with a p < 0.05 were considered statistically significant.

Results: Six patients were operated for BOM, mean age at surgery 63 (range 49-77); 50 patients were operated for EOC mean age at surgery 65 (range 51-78) 10 mean age of 58 (range 25-67). BOM had 10 fold or higher than normal expression of miR-1290, miR-520c-3p, miR-155, miR-645, miR-576-3p while EOC 10 fold or lower than normal expression of the same miRs (p < 0.05).

Conclusions: Plasma miRNA pattern reliably distinguishes benign pelvic masses from ovarian cancer. If our pilot study is replicated in the validation cohort this method microRNA patterns will become a reliable biomarker of ovarian cancer detection in patients presenting with pelvic masses.
Brief Communications on Ovarian Cancer

TRANSIENT SUPPRESSION OF P53 FOLLOWED BY TRANSDUCTION OF DEFINED ONCOGENES CONVERTS OVARIAN STEM-LIKE CELLS INTO TUMOR-INITIATING CELLS

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Background: Cancer stem cells may be integral to the development and progression of human cancers. Although the existence of tumor-initiating cells (T-ICs) in several types of human cancer has been documented, the contribution of somatic stem cells to the development of T-ICs has remained unclear.

Methods: FACS-sorted EpCAM-expressing cells in mouse ovaries were assessed for their stem cell properties using in vitro assays. In addition, EpCAM-expressing cells were transfected with p53 siRNA before their infection with defined oncogenes. The transformed cells were orthotopically transplanted into immunocompetent recipient mice. To investigate whether the established ovarian tumors are organized as hierarchies of cells sustained by T-ICs, EpCAM-expressing tumor cells were evaluated for their cancer stem cell characteristics.

Results: Normal mouse ovary contained EpCAM-expressing cells that possess the ability to differentiate into cytokeratin 8-expressing epithelial progeny cells. Furthermore, transient depletion of p53 followed by retrovirus-mediated transfer of c-Myc and K-Ras oncogenes in EpCAM-expressing cells resulted in the generation of ovarian T-ICs. The established ovarian T-ICs gave rise to hierarchically organized lethal tumors in vivo and were able to undergo peritoneal metastasis. Finally, subsequent RNA interference-mediated knockdown of p53 in tumor cells triggered the expansion of EpCAM-expressing cancer stem cells and induced further tumor growth.

Conclusions: These data revealed a role for p53 in the development and expansion of ovarian cancer stem cells, and provided strong support for the concept of “cancer stem cell targeted therapy” to eradicate ovarian cancer.
Brief Communications on Ovarian Cancer

DYNAMIC CHANGES IN CIRCULATING TUMOUR DNA OCCUR MORE RAPIDLY THAN CA125 FOLLOWING TREATMENT WITH CHEMOTHERAPY IN PATIENTS WITH OVARIAN CANCER

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Background and aims: Better early markers of response are required in patients with ovarian cancer. The TP53 gene is mutated in 97% of high-grade serous ovarian cancer (HGSOC) and can be detected as circulating tumour DNA (ctDNA) in blood. We correlated changes in TP53 mutated ctDNA with CA125 changes in 39 patients undergoing chemotherapy for HGSOC.

Methods: We extracted the DNA and sequenced TP53 from archival FFPE samples and designed mutation specific Taqman probes to accurately quantify levels of mutant TP53 ctDNA using microfluidic digital PCR. We compared levels of ctDNA to CA125.

Results: To date we have detected ctDNA carrying tumour-specific TP53 mutations at ≥40 amplifiable copies per ml of plasma in 27 of 39 cases (72%). Levels of ctDNA showed substantially faster response times compared to CA125. Of 29 chemotherapy episodes available for analysis at relapse, 8 showed a 50% reduction in ctDNA, 7 showed a 50% reduction in CA125 and 14 showed a 50% reduction in both. Median time to ctDNA response was 21 days earlier than CA125.

Conclusion: We have developed an effective method for analysis of ctDNA in patients with HGSOC. Circulating tumour DNA shows promise as an early response biomarker with more rapid dynamic changes compared with CA125.
Brief Communications on Ovarian Cancer

BREAST CANCER IS A SIGNIFICANT RISK FACTOR FOR THE SUBSEQUENT DEVELOPMENT OF OVARIAN CANCER

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In the present paper we studied the risk factors of second primary ovarian cancer in breast cancer patients. We identified 13,386 women operated on between 1999 and 2007 for a first primary invasive cancer of the breast. Second primary ovarian cancer was the event of interest. Survival analysis with competing events was applied. Standardized incidence ratios (SIRs) were computed. After a median follow-up of 60 months, 26 ovarian cancers were observed, corresponding to a 5-year cumulative incidence of 0.18%. Women with a first-degree breast cancer family history had a higher risk of developing a second primary ovarian cancer compared to women with a second-degree or no familiarity (P-value P< 0.01). Overall, we observed an incidence of ovarian cancer in the breast cancer population compared to the one expected from the general population (SIR of 1.83; 95% CI 1.20-2.68). BC patients aged 40 to 49 years were associated with a SIR of 3.13 (95% CI 1.50-5.75). Also, BC patients with a first-degree family history of BC had a significantly increased risk of ovarian cancer compared to the general population, with a SIR of 5.00 (95% CI 2.39-9.19) while patients with a second-degree or no family history had a SIR of 1.14 (95% CI 0.59-2.00). Patients aged 40-49 with a first-degree family history had a SIR of 13.3 (95% CI 3.6-34.1). Our results suggest that young breast cancer patients, reporting a first-degree family history of breast cancer, are at high risk for ovarian cancer and deserve special gynecological surveillance.
Brief Communications on Ovarian Cancer

BEVACIZUMAB BEYOND PROGRESSION IS NOT ASSOCIATED WITH PROLONGED PROGRESSION-FREE SURVIVAL IN EPITHELIAL OVARIAN CANCER

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Objective: To evaluate the efficacy and safety of bevacizumab beyond progression (BBP) in patients with epithelial ovarian cancer (EOC).

Methods: A multicenter retrospective analysis of patients with EOC who received bevacizumab was conducted. Patients who were treated with front-line bevacizumab and recurred were separated based on whether they received any treatment with BBP:

1. No further bevacizumab
2. BBP at first or second recurrence (BBP₁/₂);
3. BBP at third or fourth recurrence (BBP₃/₄).

Another group consisted of those who did not receive front-line bevacizumab, but were treated with bevacizumab at first recurrence. Progression-free (PFS) and overall survival (OS) were analyzed using Kaplan-Meier method and Cox proportional hazards model.

Results: 385 eligible patients were identified. 81 patients received front-line bevacizumab, subsequently recurred, and received either:

1. No BBP treatment (69%; n=56);
2. BBP₁/₂ (22%; n=18); or
3. BBP₃/₄ (9%; n=7).

65 patients did not receive bevacizumab until first recurrence. There was no difference in OS between the treatment groups. However, PFS was statistically superior in the group that did not receive BBP compared to those treated with BBP₁/₂ (11 vs 7 months; p=0.04); or BBP₃/₄ (11 vs 8 months; p=0.01); or those who did not receive bevacizumab until first recurrence (11 vs 5 months; p=0.01).

Conclusions: These findings do not suggest that continued VEGF inhibition with bevacizumab beyond PD is useful in the management of previously bevacizumab-treated patients with EOC. However, there may be a PFS benefit toward using bevacizumab front-line rather than reserving this therapy for first recurrence.
Brief Communications on Ovarian Cancer

RISKS AND BENEFITS OF SCREENING ASYMPOMATIC WOMEN FOR OVARIAN CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Screening asymptomatic women could potentially reduce mortality from ovarian cancer but may also cause harm. We performed a systematic review and meta-analysis to quantify risks and benefits of ovarian cancer screening.

Methods: We searched MEDLINE, EMBASE, CINAHL, and CENTRAL up to Feb. 5, 2012. Eligible studies enrolled asymptomatic women and assigned them to screening for ovarian cancer or usual care. Bibliographies were screened for additional eligible studies. Two reviewers independently screened studies for eligibility and abstracted data regarding demographic information, methodology, and patient-important outcomes.

Results: Ten RCTs and three prospective cohort studies proved eligible. Screening did not reduce all-cause mortality (RR=1.0, 95%CI 0.96-1.06), ovarian cancer specific mortality (RR=0.84, 95%CI 0.37-1.91), or reduce the risk of diagnosis at an advanced stage (RR of FIGO stage 3-4=0.86, 95%CI 0.68-1.11). Screening of any type led to a mean of 9.1 surgeries to detect one case of ovarian cancer (95%CI 6.3-16.7). Sub-group analysis based on type of screening found trials using only transvaginal ultrasound resulted in a mean of 50 surgeries per ovarian cancer detected (95%CI 33.3-100), while screening with CA-125 led to 3.4 surgeries per ovarian cancer detected (95%CI 2.8-4.8). Surgery was associated with severe complications in 2.9-8.7% of women. Quality of life was not affected by screening; however women with false-positive results had increased worry compared to those with normal results (OR=2.8, 95%CI 1.1-7.2).

Conclusions: Screening low-risk asymptomatic women for ovarian cancer does not significantly reduce mortality or diagnosis at an advanced stage and is associated with unnecessary surgery.
Brief Communications on Ovarian Cancer

WHAT DO 676 OVARIAN CANCER (OC) PATIENTS EXPECT FROM THEIR DOCTORS AND THERAPY MANAGEMENT? A GERMAN SURVEY OF THE NOGG

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Background: The primary aim of this study was to investigate information needs and preferences among patients with ovarian cancer, focusing especially on doctor-patient relationships and therapy management.

Patients and methods: A 42-item questionnaire was developed and validated in a mono-centre phase-I study and was then provided to primary and recurrent ovarian cancer patients via internet (online) or as a print-version. In the first part basic data (age, tumour status, therapy) were requested. In the second part, most of the questions try to evaluate the expectations and needs concerning their therapy management and doctor-patients communication.

Results: A total of 676 (201 online; 475 print version) patients with ovarian cancer from 44 German centres took part in the survey from January to November 2009.

The median age of the online group was 49 years (range 19-84), for the print group 62 years (26-92). Nearly all patients (98.7%) had a primary surgery and a primary chemotherapy (89%). Asked for side effects during therapy, the most frequent answers were alopecia, paraesthesia/dysaesthesia and fatigue. The three most important aspects, which were proposed by patients to improve therapy against ovarian cancer were: “Doctors should have more time for explanations”, “The therapy should not lead to any loss of hair” and “The therapy should be more effective”.

Conclusions: This study underlines the high need of ovarian cancer patients to discuss all details concerning treatment options and clinical management. As matter of fact, the physician involved in the treatment is the most important source of information.
Brief Communications on Ovarian Cancer

NANOFLUIDIC TECHNOLOGIES IDENTIFY CLINICAL FEATURES OF NEOADJUVANT TREATMENT AND OUTCOMES IN OVARIAN CANCER

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Objective: Neoadjuvant chemotherapy is used in treating advanced ovarian cancer. We determined the impact of chemotherapy on gene and microRNA expression in these specimens using nanofluidic technology. RNA extraction validated the technique from archival formalin-fixed paraffin-embedded tissue.

Methods: 78 consecutive advanced ovarian cancer patients treated with primary surgical debulking versus neoadjuvant chemotherapy (15/78) were investigated. All neoadjuvant patients were treated with combination platinum and Taxol. A chip 48.48 analyzed panel of 96 potential predictors of response to chemotherapy. All samples were normalized for multiple housekeeping genes. Each factor was categorized as high/low expression using the mean value as cutoff. Overall survival was analyzed using Kaplan and Meier method.

Results: We assessed impact of neoadjuvant chemotherapy on selected genes and microRNAs. Among cell growth and proliferation, genes MKI67, PLK1, PBK were reduced. Deactivation of TUBB3 survival pathway was reduced, while its negative regulator GNAI1 was increased. ERBB2 resulted downregulated in the neoadjuvant setting, while HGF and PTEN increased. MicroRNAs expression broadly increased, with only the exception of miR-20a and miR-141. Patients exhibiting high levels of COL11A1 and PLK1 were poor performers, while the opposite occurred for GLI1. At the micro-RNA level the best predictors (miR-193a-5p, miR-375, miR-20a). The poor performers (miR-193a-5p, miR-375) were featured by high levels of micro-RNA while the opposite for miR-20a.
Conclusions: The nanofluidic platform may provide deeper insight into specific roles of clinically relevant major molecular networks. Chemotherapy induced modification of genes and microRNA expression can be a model to develop future prognostic biomarkers and therapeutic modalities.
Brief Communications on Ovarian Cancer

EXPLORATORY STUDY OF PLATINUM-SENSITIVE (PS) PATIENTS WHO DID NOT ACHIEVE A COMPLETE RESPONSE AFTER FIRST-LINE PLATINUM-BASED TREATMENT BEFORE OVA-301 TRIAL

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Background: A randomised phase III OVA-301 trial compared the efficacy and safety of trabectedin plus pegylated liposomal doxorubicin (PLD) vs. PLD in 672 patients with recurrent ovarian cancer (ROC) after failure of first-line platinum-based chemotherapy. Trabectedin/PLD significantly improves progression-free survival (PFS) and overall response rate (ORR).

Methods: This exploratory analysis evaluated the outcomes in patients with PS (platinum-free interval [PFI] ≥6 months) ROC who, according to investigator assessment for best response, did not reach a complete response (CR) after first platinum-based therapy. The analysis of PFS and ORR observed during OVA-301 was based on independent oncologist assessment, which combined radiological assessment with clinical and laboratory data. OS was defined from randomization to death/last contact.

Results: Among the 430 patients in PS stratum, 178 (41.4%) patients did not reach a prior CR: 93 in the trabectedin/PLD arm and 85 in the PLD arm. Median PFS was 9.6 months with trabectedin/PLD vs. 5.5 months with PLD (hazard ratio [HR]=0.61; 95%CI: 0.42-0.89; p=0.0089). ORR was 38.0% for trabectedin/PLD vs. 16.5% for PLD (p=0.0014), while the disease control rate (ORR + stable disease lasting ≥3 months) was 71.7% vs. 56.5% (p=0.0474), respectively. The median OS was 25.0 months with trabectedin/PLD vs. 19.4 months with PLD (HR=0.69; 95%CI: 0.49-0.97; p=0.0315). The safety of trabectedin/PLD in this subset was similar to that of the overall population.

Conclusions: Results suggest an enhanced benefit of trabectedin/PLD in this subpopulation, being an important option in the treatment of ROC.
Brief Communications on Uterine Cancer including Sarcoma

MANAGEMENT OF ATYPICAL ENDOMETRIAL HYPERPLASIA AND EARLY ENDOMETROID ADENOCARCINOMAS WITH LEVONORGESTREL INTRAUTERINE DEVICE IN MORBIDLY OBESE AND HIGH-RISK SURGICAL CANDIDATES

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Objective: To investigate the efficacy of levonorgestrel intrauterine device (IUD) in treatment of atypical endometrial hyperplasia and early stage, grade 1 and 2 endometroid adenocarcinoma.

Study design: 8 patients with endometroid adenocarcinoma (Grade 1 and 2; 5 and 3 respectively) and 7 patients with atypical hyperplasia with morbid obesity or severe co-morbidities were treated with levonorgestrel intrauterine device over 2 years. All patients had a hysteroscopy, dilatation and curettage for diagnosis. Preoperative and 3 to 6 month postoperative endometrial stripes were acquired. At least 1 endometrial biopsy was obtained postoperatively.

Results: There was resolution of atypical hyperplasia and endometroid adenocarcinoma in all patients with Progesterone effect in 14 and simple hyperplasia without atypia in one. Revised cardiac index class ranged between Class III - IV (6.6 - 11% perioperative cardiac risk). Mean Body mass index was 47.5 (range 33.8 to 73). Mean pre and postoperative endometrial stripes on transvaginal ultrasound (TVS) were 11.25mm and 5.19 mm respectively and correlated well with pathological resolution. A meta-analysis of 13 published studies with adequate data was performed. A total of 147 atypical hyperplasias and 19 low grade endometrial cancers were treated with a progestational IUD. Complete pathological response was observed in 157 of 166 (94.5%). There were 7 partial responses and 1 patient with progression.

Conclusion: Levonorgestrel IUD is an effective treatment option for morbidly obese high surgical risk patients and TVS evaluation of endometrial stripe is a useful follow up tool.
Brief Communications on Uterine Cancer including Sarcoma

A MULTI INSTITUTIONAL CLINIC-PATHOLOGIC STUDY OF UTERINE SEROUS CARCINOMA WITHOUT MYOMETRIAL INVASION


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Introduction: To analyze the clinico-pathologic factors in patient with uterine serous carcinoma (USC) without myometrial invasion.

Materials and methods: 236 USC from 4 institutions were reviewed by gynecologic pathologists. 50 cases were reviewed as a group for consistency in the diagnosis. Patients' age, tumor size (≤2 versus > 2 cm), myometrial invasion, lymphovascular invasion (LVI), lymph node (LN) status, tumor location (endometrium vs polyp), cervical involvement, FIGO stage, pelvic washings, and recurrence were studied.

Results: 55 (23%) had tumors with no myometrial invasion. The mean age was 68.7 years. 44 (80 %) patients had stage IA tumors, 1 patient (1.8%) had stage II, 1 patient had stage IIIA (1.8%), and 9 (16.4%) had stage IVB. The tumor was confined to a polyp in 17 (30.9 %) patients, while in 19 (34.5%) patients, tumor was detected in the endometrium and polyp. 19 patients (34.5%) had tumors larger than 2 cm and 12 (21.8%) exhibited LVI. 3 patients (5.4 %) had cervical involvement. 2 (3.6%) patients had LN involvement and 7 (12.7%) had positive washings. 8 patients (14.5 %) experienced recurrence. In patients with tumor confined to a polyp, 5 (29.4%) were stage IVB, 11 (64.7 %) had tumors > 2 cm in size, 1 (5.9%) had LVI, 3 (17.6%) had positive washings, and 3 (17.6%) stage IVB patients recurred.

Conclusion: USC without myometrial invasion, even when confined to a polyp, can be associated with poor prognostic factors, further stressing the importance of complete surgical staging and adjuvant treatment in this setting.
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SIRTUIN1 (SIRT1), A LONGEVITY GENE, IS OVER-EXPRESSED IN ENDOMETRIAL CARCINOMA

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Background: Sirtuin 1 (SIRT1) is one of the NAD-dependent histone deacetylase, and known as a longevity gene induced by caloric restriction. SIRT1 is also thought as a tumor suppressor gene. However, the overexpression of SIRT1 in various cancers was reported with undetermined significance. Therefore, we examined the expression of SIRT1 in normal and neoplastic endometria to clarify the role on endometrial carcinogenesis.

Methods: The expressions of SIRT1 and Ki67 were examined by indirect immunohistochemical staining using formalin-fixed tissue specimens of 110 endometrial carcinomas, 72 normal endometria and 24 endometrial hyperplasias. Immunoreactivity was evaluated according to the ratio of positive cells in 200 cells and described as a positivity index (PI, full score 100). In addition, the expressions of SIRT1, p53, PCNA in endometrial carcinoma tissues or cell lines were examined using Western blotting.

Results: The expression of SIRT1 of carcinoma (PI=37.0±25.6) was significantly higher than that of normal endometrium (PI=25.3±26.5) (P= 0.006). In carcinoma, the expression of SIRT1 was significantly higher in grade 3 tumors (P= 0.006) and the tumors with lympho-vascular space invasion (P= 0.044). However, the significant correlation between SIRT1 and Ki67 expression was not observed (P=0.051). The expressions of SIRT1 were inversely correlated with that of p53 in carcinoma tissues and cell lines.

Conclusions: These results suggested that SIRT1 is rather positively involved in endometrial carcinogenesis and progression through down-regulation of p53. Further studies are needed to clarify the role of SIRT1 in endometrial carcinoma.
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A COMPARISON OF UTERINE PAPILLARY SEROUS, CLEAR CELL CARCINOMAS, AND GRADE 3 ENDOMETRIOID CORPUS CANCERS USING THE REVISED FIGO STAGE


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Objective: This study was designed to compare the survival outcomes of patients with UPSC or CC to those of patients with G3EC according to the old and revised FIGO staging systems.

Methods: We retrospectively reviewed all patients with endometrial cancer treated at a single institution between 1995 and 2009. Among the 647 patients with endometrial cancer, 46 with G3EC and 45 with UPSC/CC histology were confirmed.

Results: FIGO 88 stage, FIGO 09 stage, and extrauterine metastasis were significantly different between the UPSC/CC and G3EC groups (P < 0.001, P = 0.004 and P = 0.004, respectively). Restaging from the FIGO 88 to the FIGO 09 criteria increased the number of stage I cases by 10 (11.0%). Overall, 8 patients in the UPSC/CC group were down-staged to stage I, and 2 patients in G3EC were down-staged to stage I. The 5-year disease-specific survival (DSS) was 43.5% vs. 72.6% (P = 0.031), and progression-free survival (PFS) was 57.4% vs. 79.8% (P = 0.047) in the UPSC/CC and G3EC groups, respectively. In univariate analysis, a histologic type of UPSC/CC, a FIGO 09 stage of III-IV, and positivity for LVSI were negatively associated with PFS, as well as with DSS. In multivariable analysis, UPSC/CC cell type, a FIGO 09 stage of III-IV, and LVSI were independent factors for DSS.

Conclusion: We observed that UPSC and CC histotypes might entail a worse survival outcome than G3EC in the 2009 FIGO staging system.
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BRCA1 IMMUNOHISTOCHEMICAL STAINING AS A PROGNOSTIC INDICATOR IN UTERINE SEROUS CARCINOMA

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Objectives: To investigate the relationship between BRCA1 protein expression, as determined by immunohistochemistry, and clinical outcome in uterine serous carcinoma.

Methods: A tissue microarray (TMA) containing duplicate cores of 73 cases of uterine serous carcinoma was immunohistochemically stained with an antibody against BRCA1. The cores were scored in a semiquantitative manner evaluating both the distribution and intensity of nuclear staining. BRCA1 protein expression was correlated with progression free survival (PFS) by multivariate analysis.

Results: Fifty nine of 73 cores were evaluable and there was a statistically significant inferior PFS of those cases exhibiting staining of 76-100% of tumour cell nuclei, compared to the other cases (p=0.0023).

Conclusions: Our study illustrates that low level of BRCA1 protein expression is a favourable prognostic indicator in uterine serous carcinoma; this is similar to the situation in ovarian high grade serous carcinoma. Further studies should investigate the BRCA status of uterine serous carcinomas at a molecular level and assess whether BRCA1 protein expression correlates with response to chemotherapy in uterine serous carcinoma.
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**ONCOLOGIC AND REPRODUCTIVE OUTCOMES OF WOMEN UNDERGOING PROGESTIN THERAPY FOR COMPLEX ATYPICAL HYPERPLASIA OR GRADE 1 CARCINOMA OF THE ENDOMETRIUM**

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**Objective:** The aims of this study were to evaluate oncologic and fertility outcomes in young women with complex atypical hyperplasia (CAH) or grade 1 endometrial carcinoma (EM) treated with progestin therapy.

**Methods:** This retrospective review included women less than 45 years of age with CAH or EM who desired fertility-sparing treatment. Medical records were reviewed for demographics, pathologic and treatment information. Institutional IRB approval was obtained for this study. Statistical analyses were performed using Fisher exact test, Pearson χ² test, and Spearman rank correlation test.

**Results:** Of the 75 patients identified, 23 (13-CAH, 10-EM) were included who met inclusion criteria and for whom records were available. There were no significant differences between the CAH and EM groups. The average age was 38.5 ± 4.35 in the CAH group and 38.5 ± 4.17 in the EM group (p=0.98). BMI was not correlated with severity of pathology (rₛ = -0.0972, p = 0.69). Treatment was split between oral progestosterone only, levonorgestrel intrauterine device (IUD) only and both oral and intrauterine progesterone. After a median follow-up of 13 months, 9 patients had persistent or progressive disease. Eight patients ultimately had hysterectomy. No patient was found to have disease outside the uterus. Median time from diagnosis to hysterectomy was 13 months. Fourteen patients ultimately underwent ART. Of these, 2 received care outside our center and both ultimately had children via gestational surrogate. Twelve had IVF in our center, eight (61.5%) in the CAH group, 4 (40%) in the EM group (p=0.08). Five clinical intrauterine pregnancies (42%) and 4 live births (33%) resulted.

**Conclusion:** Fertility-sparing treatment for CAH and grade 1 endometrial cancer is possible. Our data is consistent with regression rates reported in the literature. Patient selection requires highly motivated patients who will adhere to treatment and follow-up recommendations.
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METFORMIN USE IS ASSOCIATED WITH IMPROVED DISEASE FREE SURVIVAL IN PATIENTS WITH ENDOMETRIOID ADENOCARCINOMA

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Purpose: Recent data have demonstrated that metformin use may improve outcomes in patients with a variety of cancers including pancreas, ovarian, and breast cancer. The purpose of this study was to determine whether metformin use was associated with improved survival in patients who underwent surgery with or without adjuvant therapy for endometrioid adenocarcinoma (EAC).

Methods: A retrospective study of patients with EAC who received hysterectomy at the University of Pennsylvania between 1991 and 2009 was performed. Information regarding diabetes history and medication usage was abstracted from patient charts. Survival analysis was performed using the Kaplan-Meier method, log-rank test, and Cox proportional hazards regression models.

Results: 422 patients were identified. Stage breakdown was as follows: IA (229), IB (102), II (25), IIIA (31), IIIB (2), IIIC (31), IV (2). 238 patients received adjuvant radiotherapy (RT): external beam RT alone (90), vaginal brachytherapy (96), or both (52). 51 patients received chemotherapy. 63 patients had diabetes, 22 were on metformin. Disease free survival (DFS) at 5 years was 95%, 65%, and 84% for diabetic patients on metformin, diabetic patients not on metformin, and non-diabetic patients, respectively, p = 0.02. There was no difference in overall survival based on metformin usage. Patients on metformin had a 35% lower risk of recurrence, HR was 0.65 (95%CI 0.43-0.99, p = 0.046), after adjusting for other clinical pathologic predictors including stage, lymphovascular invasion, and pathologic grade.

Conclusion: Metformin use at the time of hysterectomy in patients with endometrioid adenocarcinoma resulted in improved DFS. Future studies should prospectively evaluate metformin in this population.
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ROBOTIC SINGLE PORT LAPAROSCOPY FOR ENDOMETRIAL CANCER PATIENTS: PRELIMINARY EXPERIENCE

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Objective: We present the technique to perform single access robotic laparoscopy for endometrial cancer patients.

Methods: Four patients with histological diagnosis of endometrial adenocarcinoma G1 and instrumental FIGO stage IA or IB underwent total single access robotic laparoscopic extra-fascial hysterectomy and bilateral salpingo-oophorectomy. Procedure was performed through a single trans-umbilical incision of 35 mm using Da Vinci Robotic S-System and Gelport device with one 12 mm trocar for robotic 3D optic, two 8-mm trocars and one 5-mm trocar. Surgeries followed the classic laparoscopic technique using 12 mm 0 degree robotic camera, EndoWrist bipolar forceps, EndoWrist monopolar scissor, EndoWrist needle holder and laparoscopic suction irrigation and grasper. Vaginal cuff was repaired with an intra-corporeal suture using a barbed wound closure system.

Results: The planned surgical procedures were successfully completed. Two G1, endometrial cancer FIGO stage IA and two IB were treated. Median BMI was 25.65 (range, 22 to 29.3). Median total operative time was 183 minutes (range, 160 to 250). Median docking time was 14 minutes (range, 11 to 17 minutes). Median blood loss was 50 mL (range, 10 to 90 mL). No cases required multiple abdominal access. None of the patients were converted to laparoscopy or laparotomy. No intra-operative or postoperative complications occurred. All patients were discharged on day two.

Conclusions: Robotic single-port trans-umbilical total hysterectomy and bilateral salpingo-oophorectomy is technically feasible and reproducible in patients with low-stage endometrial cancer. Despite encouraging results regarding surgical outcome and postoperative course, additional studies are needed to demonstrate benefits of this technique.
TELOMERE MAINTENANCE IN ENDOMETRIAL CANCERS: TELOMERASE OR ALTERNATIVE LENGTHENING OF TELOMERES?

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Objective: To study the telomere maintenance mechanism in endometrial carcinoma, endometrial hyperplasia, and normal endometrium, and to evaluate their relation with carcinogenesis and progression of endometrial carcinoma.

Methods: Telomerase activity, hTERT expression, and alternative lengthening of telomeres (ALT) status were determined in 131 endometrial samples (85 cases of endometrial cancer, 16 cases of endometrial hyperplasia, and 30 cases of normal endometrium) by telomeric repeat amplification protocol (TRAP), immunohistochemical method, and APB assay.

Results: In TRAP assay, 52 endometrial cancer samples (61.2%), 9 cases of endometrial hyperplasia (56.3%), and 10 cases (33.3%) of normal endometrium demonstrated increased levels of telomerase activity. Immunohistochemical staining for hTERT was present in 43 (50.6%) of endometrial cancer and none of endometrial hyperplasia samples and normal endometrial tissues. ALT status according to APB assay showed positive results in 15 (17.6%) patients. Whereas increased telomerase activity was not associated with stage or prognosis but with grade and histology, ALT status was correlated with prognosis as well as grade and histology.

Conclusion: Telomere maintenance mechanisms are closely correlated with the grade and histologic type of endometrial cancer. ALT may play an important role in the regulation of endometrial cancer progression and high grade histology.
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CERVICAL CYTOLOGY IN SEROUS AND ENDOMETRIOID ENDOMETRIAL CARCINOMA

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Objective: To determine the incidence of abnormal cervical cytology in patients diagnosed with uterine papillary serous carcinoma (UPSC) and endometrioid endometrial carcinoma (EEC). Additionally, associations between abnormal cervical cytology and clinicopathological factors were evaluated.

Setting: Radboud University Nijmegen Medical Centre, Canisius Wilhelmina Hospital, Rijnstate Hospital Arnhem, Gelderse Vallei Hospital Ede, and Maas Hospital Boxmeer, the Netherlands.

Population: EEC patients diagnosed at two hospitals from 1999-2009, and UPSC patients diagnosed at five hospitals from 1992-2009 were evaluated.

Methods: Cervical cytology within six months before histopathological diagnosis of endometrial carcinoma was available for 267 EEC and 80 UPSC patients. Cervical cytology with atypical, malignant, or normal endometrial cells in post-menopausal women was considered as abnormal cytology, specific for endometrial pathology.

Main outcome measures: Clinicopathological variables associated with abnormal cervical cytology.

Results: Abnormal cervical cytology was found in 87.5% of UPSC patients, compared to 37.8% in EEC patients. In UPSC, abnormal cytology was associated with extra-uterine spread of disease ($P = 0.043$). In EEC, abnormal cytology was associated with cervical involvement ($P = 0.034$). In both EEC and UPSC patients abnormal cervical cytology was not associated with survival.

Conclusions: The high incidence of abnormal cytology specifically in UPSC patients, together with the association with extra-uterine disease and with cervical involvement in EEC patients, might indicate that more extensive surgery may be anticipated when abnormal endometrial cells are found in pre-operative cervical cytology.
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TUBULIN-B-III OVEREXPRESSION BY UTERINE SEROUS PAPILLARY CARCINOMAS IS A MARKER FOR POOR OVERALL SURVIVAL, PACLITAXEL RESISTANCE AND SENSITIVITY TO EPOTHILONES

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Introduction: Uterine serous papillary carcinoma (USPC) represents an aggressive variant of endometrial cancer. Despite morphologic similarity to ovarian serous papillary carcinomas (OSPC), growing clinicopathologic and genetic evidence supports the distinctness of these entities. Tubulin-β-III overexpression prognosticates poor outcome in many cancers but has been incompletely described in USPC. Epothilones are microtubule-stabilizing agents with activity in paclitaxel-resistant malignancies.

Objectives: To characterize in vitro chemosensitivity to paclitaxel/patupilone and correlate survival in relationship to tubulin-β-III expression in USPC versus OSPC.

Methods: Tubulin-β-III was quantified by RT-PCR in fresh-frozen specimens (28-USPC/20-OSPC) and cell lines (7-USPC/7-OPSC), and correlated with immunohistochemistry (IHC) (n=17). Copy number was used to stratify overall survival (OS). IC₅₀ was determined in cell lines (8-USPC/4-OSPC). Impact of tubulin-β-III knockdown on IC₅₀ was assessed using siRNAs.

Results: Table 1 illustrates source specimen characteristics. USPC overexpressed tubulin-β-III relative to OSPC in fresh-frozen tissue and cell lines (Figure 1a/b). IHC reflected RT-PCR copy number (Figure 2a). Tubulin-β-III overexpression stratified poor OS (Figure 2b). Relative to OSPC, USPC were more sensitive to patupilone (IC₅₀ 0.24±0.11 nM versus 0.83±0.21 nM, p=0.04)(Figure 3a). Tubulin-β-III expression correlated with paclitaxel resistance, and knockdown enhanced in vitro sensitivity to paclitaxel (Figure 3b/c).

Conclusions: Tubulin-β-III is overexpressed by USPC relative to OSPC and is a marker for reduced OS, paclitaxel resistance, and sensitivity to patupilone. Epothilones represent a promising treatment strategy for USPC.
Table 1: Source patient characteristics for fresh-frozen tissue samples.

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Age, mean [range] (y) 69.2 [36-88] 60.8 [33-90]

Figure 1. Uterine serous papillary carcinomas overexpress tubulin-β-II relative to ovarian serous papillary carcinoma. Tubulin-β-II expression as determined by RT-PCR (x-axis) is plotted for uterine papillary serous (UPSC) and ovarian serous papillary (OSPC) carcinomas in (a) fresh frozen tissue (20 OSPC, 28 UPSC) and (b) chemo-naive cell lines (7 OSPC, 7 UPSC). Mean ± SEM is shown.
Figure 2. [a] IHC staining correlates with tissue expression determined by RT-PCR. Representative slides are shown relative to copy number. Mean score for USPC versus OSPC was 3+ versus 0-1+, respectively, \( p=0.002 \). [b] Tubulin-β-III expression by RT-PCR stratifies overall survival among patients with USPC.
**Figure 3.** [a] Uterine serous papillary carcinomas are highly sensitive to patupilone (blue dotted) compared to paclitaxel (black solid) and in relation to ovarian serous papillary carcinomas. Representative dose-response curves are shown for USPC-ARH-1, 2, 3, 7 and OSPC-1, 2, 3, 5. [b] Knockdown of tubulin-β-III increases sensitivity to paclitaxel. Dose-response curves are shown for cells treated with mock (black solid) and tubulin-β-III (blue dotted) siRNA. [c] Tubulin-β-III copy number correlates with paclitaxel resistance. Data shown for USPC-ARH-3, 5, 14, 15.
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ANALYSIS OF THE SPECT-CT ACCURACY IN THE SENTINEL LYMPH NODE BIOPSY IN ENDOMETRIAL CANCER

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Introduction: The use of sentinel lymph node biopsy (SLNB) in endometrial cancer regards patients with high risk of nodal metastases. In patients with no metastases lymphadenectomy provides no benefit and solely increases risk of complications. Thus identification of negative sentinel lymph nodes (SLNs) could result in abandoning unnecessary lymphadenectomy.

Aim of study: Aim of the study was to evaluate accuracy of SPECT-CT in SLNB in endometrial cancer.

Material and methods: From February 2011 to March 2012, 40 patients with endometrial cancer underwent SLNB using four detection techniques: SPECT-CT, gamma probe, blue dye, and combined technique (gamma probe and blue dye). Tc-99m radiocolloid albumin was administered to the cervix and the blue dye in subserosal injection to the fundus.

Results: SPECT-CT revealed active spots in 37 patients (92.5%). Using combined technique and handheld probe detection rate was 97.5%. Bilateral SLN detection was achieved in 72.5% in combined technique and 70% using SPECT-CT. Accuracy rate of SPECT-CT in study population was 93.3% (mean value of active spots and number of hot SLNs ratio calculated for every patient). In 36 women (90%) there was complete concordance of SPECT-CT and intraoperative SLN detection. In 96 resected SLNs, there was 1 positive node. There was one metastasis in non-sentinel lymph nodes in the only patient without detected SLN.

Conclusions: Presented series confirms that SLNB in endometrial cancer is feasible and provides correct information on nodal status. Combined cervical and subserosal tracers administration constitutes an optimal detection method. The SPECT-CT correctly predicts sentinel lymph nodes localization.
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LIPOSOMAL DOXORUBICIN (NPLD) AND CARBOPLATIN IN PRIMARY ADVANCED OR RECURRENT ENDOMETRIAL CANCER - A PHASE-II-TRIAL OF AGO AUSTRIA

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Introduction: Endometrial carcinoma with recurrence or advanced stage carries a poor prognosis. Chemotherapy is used more frequently, consisting of cisplatin/doxorubicin/paclitaxel, if tolerated, or the doublet of carboplatin/paclitaxel.

These are the final results 39 patients from an Austrian AGO trial of NLPD and Carboplatin in patients with primary advanced or relapsed endometrial cancer. Primary endpoint is RR (response rate), second endpoint is feasibility.

Methods: 39 patients were recruited in this trial. All patients received 60mg/m² N PLD and Carboplatin AUC 5 for 6-9 cycles or until progression. First analysis after 23 patients showed the combination to be active. The trial was stated to be successful with >14 responses in the final analyses and feasible with ≥50% of patients receiving ≥6cycles.

Results: At baseline, 18 (46%) patients had stage I tumor, 1 (3%) stage II, 9 (26%) with stage III and 11 (28%) patients with stage IV. 8 (21%) tumors with grade I, 13 (33%) grade II and 18 (46%) grade III tumors were diagnosed. Of all 39 patients 13 (33%) had primary advanced, 26 patients (67%) recurrent disease. Tumors were found to be adenocarcinomas in 29 (75%), serous papillary carcinomas in 6 (15%) cases, clearcell- and mixed mullerian carcinomas in 2 (5%) case each.

RR was defined as best response during therapy. We observed 1 (3%) complete response and partial response in 15 (38%) patients. Of 183 cycles administered 5 (13%) patients received 9, 17 (44%) patients 6 cycles of chemotherapy.

Discussion: In the final analysis the combination demonstrates activity and the endpoints of the study were met.
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CLINICOPATHOLOGICAL AND PROGNOSTIC IMPACT OF HER2 AND HORMONE RECEPTOR EXPRESSIONS IN UTERINE PAPILLARY SEROUS CARCINOMA (UPSC)


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Uterine papillary serous carcinoma (UPSC) is a rare and aggressive variant of endometrial carcinoma. Little is known about the pathologic and biologic features of this tumor. Human epidermal growth factor receptor 2 (HER2) and hormone receptor (HR) expression play important roles in tumor behavior and clinical outcome, but their relevance in UPSC is not clear. Here, HER2 and HR expression assessed by immunohistochemistry was correlated with clinicopathological parameters using Cox's univariate and multivariate analyses in 27 patients with stage I disease, 13 with stage II, 25 with stage III, and 6 with stage IV. The 5-year recurrence-free survival (RFS) and overall survival (OS) rates were 51% and 66% (67/81%, 59/77%, 43/54% and 0/0% in stages I, II, III and IV), respectively. HER2 and HR were positive in 14% (10/71) and 52% (37/71), respectively. HER2 overexpression was correlated with a lower OS rate (P = 0.01) whereas HR overexpression was correlated with a higher OS rate (P = 0.008). In multivariate models, HER2, HR, and histologic subtype were identified as independent prognostic indicators for RFS (P = 0.022, P = 0.018 and P = 0.01, respectively) but HR was the only independent factor associated with OS (P = 0.044). Thus, HER2 and HR are prognostic variables in UPSC, and HR is an independent prognostic factor for OS.
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EVEROLIMUS (E) AND LETROZOLE (L) IN WOMEN WITH PREVIOUSLY TREATED RECURRENT ENDOMETRIAL CANCER (EC): A MULTIINSTITUTIONAL PHASE II CLINICAL TRIAL

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Background: Studies using mTOR inhibition have demonstrated clinical effectiveness in women with recurrent EC. mTOR inhibition has demonstrated to be effective in overcoming hormonal resistance in some preclinical and clinical solid tumor studies.

Methods: A two institution, single arm, open-labeled, study of E (10 mg PO daily) and L (2.5 mg PO daily) was conducted in patients with recurrent EC who have failed not more than 2 prior chemotherapeutic regimens. Cycle length was 28 days; one dose reduction for E (to 5 mg) was permitted. Patients were treated until progression or toxicity. The primary endpoint was CBR (defined as RECIST v1.0), confirmed complete response (CR), partial response (PR), or prolonged stable disease (SD; ≥8 weeks).

Results: 42 patients enrolled (median age 61; range: 24-82). 7 patients were inevaluable for toxicity or response. 191 cycles have been administered. 17 of 35 (49%) evaluable patients had a CBR. The objective response rate (RR) was 20% (7 of 35). The median duration of response was: 8 mos (3-17+); 5 patients had a CR, 2 had PR and 10 had SD. 10 of 17 of these patients are still on treatment. 3 patients with CR have completed treatment and are in remission. Progression-free survival was 2.2 mos (1-17+); 12 mos non-progression rate was 37%. Median overall survival was 13 mos (1-19+). 13 patients required dose reduction of E. Most common grade 3 toxicities include: fatigue, diarrhea, thrombocytopenia. There was 1 grade 4 toxicity (anemia). Pre-existing or E-induced hyperglycemia requiring metformin was common. 9 of the 35 evaluable patients were taking metformin (4 existing users, 5 started on study). The RR for patients taking metformin was 44% (vs 12% non-users, p=0.055).

Conclusions: E and L shows encouraging CBR and RR in pretreated patients with recurrent, previously treated EC. The ability of metformin to lower circulating insulin may be important for the treatment of EC.
Brief Communications on Uterine Cancer including Sarcoma

INCREASED GENE DOSAGES OF ERBB SIGNALING NETWORK CORRELATE WITH AGGRESSIVE CHARACTERISTICS OF ENDOMETRIAL CANCER

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Introduction: Dysregulation of the ERBB signaling network occurs in many human cancers and is implicated in more aggressive tumor behavior. The data about the network and its gene dosage pattern in endometrial cancer are scarce. Therefore, the study aimed to determine clinical significance of ERBB gene dosage pattern in endometrial cancer. Additionally, components of PI3K/Akt pathway, triggered by ERBB, were examined.

Materials and methods: Study included 144 consecutive fresh frozen samples collected from stage I-IV endometrial cancer patients, both premenopausal and menopausal. ERBB1, ERBB2, ERBB3, ERBB4, PI3K and c-myc gene dosages were determined by SYBR Green-based quantitative PCR, using ΔΔCt method.

Results: Gene dosages of three receptors (ERBB2, ERBB3 and ERBB4) all correlated with each other: ERBB2 vs. ERBB3: Spearman’s ρ=0.26, p=0.002; ERBB3 vs. ERBB4: ρ=0.25, p=0.003; ERBB4 vs. ERBB2: ρ=0.56, p<0.0000001. Additionally, ERBB1 gene dosage correlated with ERBB3 (ρ=0.50, p<0.0000001). Levels of ERBB2, ERBB3 and ERBB4 were significantly higher in the subgroup with metastasis (p=0.043, p=0.0009, p=0.006, respectively). Elevated level of ERBB4 correlated with more advanced stage (p=0.0009). PI3K and c-myc gene dosages correlated with each other (p=0.62, p<0.0000001) as well as with all the ERBB gene dosages (all p<0.05).

Conclusions: Gene dosage pattern of ERBB signaling network and PI3K/Akt pathway differs in endometrial cancer depending on the stage of the disease and the presence of metastases. Examined genes seem to play a crucial role in the progression of endometrial carcinoma. Immunohistochemistry analyses of the same markers (with additional Akt examination) are planned.
Brief Communications on Uterine Cancer including Sarcoma

INTRAVENOUS LEIOMYOMATOSIS WITH INTRACAVAL AND INTRACARDIAC EXTENSION

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Objective: To explore the diagnosis and treatment of intravenous leiomyomatosis (IVL) with intracaval and intracardiac extension.

Methods: Twenty patients with surgically and histopathologically proven IVL extending to the inferior vena cava (IVC) and heart between January 2002 and April 2012 were retrospectively analyzed.

Results: The ages of the patients ranged from 24 to 49 years (42.4±7.0 years). All the patients had history of uterine leiomyoma, 16 patients (80%) had undergone an operation of uterine leiomyoma. The major clinical manifestations were pelvic masses, chest tightness and short breath, swelling in the lower extremity, palpitation, abdominal distension, syncope and skelalgia. Nine patients underwent one-stage operations, and 11 patients underwent two-stage operations. All operations were successfully performed. Among the patients finished the whole operations, complete resection of tumor was obtained in 13 (76.5%) patients, and 4 (23.5%) patients experienced incomplete resection. Seventeen patients (85%) were followed up, with a follow-up duration of 1 to 111 months (mean, 20.5 months). All the patients were survived. Recurrence occurred in 5 patients (29.4%).

Conclusions: It is important to recognize IVL with intracaval and intracardiac extension. IVL should be considered in middle-aged woman in particular with history of operation of uterine leiomyoma presenting a mass in right cardiac chambers originating from the IVC. The tumors can be removed with either one-stage or two-stage operation. Precise and full-scale pre-operative evaluation, complete tumor resection and multi-disciplinary cooperation are crucial for successful treatment.
Poster Session I

ASSESSING RISK AND MORTALITY OF VENOUS THROMBOEMBOLISM IN OVARIAN CANCER PATIENTS

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Introduction: The close two-way clinical relationship between cancer and venous thromboembolism (VTE) is well known. Ovarian cancer has a high incidence of VTE. VTE may be the first symptom of occult malignant disease and has been shown to significantly affect overall survival in patients with various cancers.

Aims: The objective of this study was to elucidate the pattern of VTE, predisposing factors, and the impact on patients’ overall survival in ovarian cancer.

Methods: We reviewed the records of all patients with ovarian cancer who were diagnosed, treated and followed up in St James’s Hospital between 2006 and 2010.

Result: The overall incidence of VTE was 9.5% (33) in 344 patients with ovarian cancer of which 48% (16) had pulmonary embolism. 11 (33%) patients developed VTE pre treatment. Eleven (33%) following surgery (1-28 day) and eleven (33%) during chemotherapy. Risk factors associated with the occurrence of VTE were age > 60 years (p< 0.05), BMI >30 (p< 0.007), clear cell carcinoma (p< 0.01), advanced stage (p< 0.01) and high grade (p< 0.01). The occurrence of VTE was associated with decreased overall survival time, with median survival time of 34.8 months for those with and 55.8 months without VTE, (p< 0.001).

Conclusion: The incidence of VTE is high in ovarian cancer especially in the clear cell cancer subtype. VTE adversely affects survival in ovarian cancer. Older age, obesity, higher tumour stage and grade and clear cell subtype could be used to establish prophylaxis protocols based on risk stratification in ovarian cancer.
WHY VENOUS THROMBOEMBOLISM IS A COMMON COMPLICATION OF OVARIAN CANCER?

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Introduction: Ovarian cancer is the leading cause of death from gynaecological malignancy and has a particular association with venous thromboembolism (VTE). The aim of this study was to measure tumor derived Tissue Factor (TF) and Tissue factor Pathway Inhibitors (TFPI) mRNA and protein and to investigate their potential role in ovarian cancer patients who develop VTE.

Methods: TF and TFPI mRNA and protein expression were measured in 100 stored tumours samples, using TaqMan PCR and ELISA assays.

Results: TF mRNA and protein expression were increased in tumours from patients with clear cell carcinoma (p< 0.0001) and endometroid carcinoma (p< 0.008) compared with benign tumours. TFPI expression was increased in clear cell carcinoma (p< 0.003) and a slight increase was observed in endometroid carcinomas. The increase in TF did not correlate with VEGF expression. TF mRNA and antigen level were increased in malignant tumours of patients who developed VTE compared with malignant tumours of patients who did not develop VTE (p < 0.01). There was no difference in TFPI or VEGF expression between the two groups.

Conclusion: The increased TF expression in ovarian cancer is associated with a higher risk of VTE. The increase in TF expression is not explained by increased angiogenesis. We consider TF derived from tumour itself as a likely trigger of VTE in ovarian cancer. TF expression was increased in clear cell ovarian cancer and endometroid cancer and this may explain the higher risk of VTE in this subgroup.
Poster Session I

ENDOGENOUS THROMBIN POTENTIAL AS A MARKER FOR VENOUS THROMBOEMBOLISM IN OVARIAN CANCER

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Introduction: Gynaecological cancers are associated with an increased risk of venous thromboembolism (VTE). Endogenous Thrombin Potential (ETP) has shown potential as a predictive marker for VTE.

Aim: To compare the procoagulant activity in plasma of patients with benign and malignant lesions of ovary using the (ETP) assay.

Patients and methods: Blood samples were obtained from 89 patients with ovarian tumours (29 benign and 60 malignant). Thrombin generation in platelet-poor plasma was measured using the Calibrated Automated Thrombography. Lag time, peak thrombin production, area under the thrombin generation curve (ETP), time to peak (TTP) were determined.

Results: Patients with ovarian clear cell carcinoma had higher peak thrombin production (p< 0.01) and greater ETP( p< 0.001) compared with benign ovarian tumours. In the neoadjuvant group peak thrombin production following thrombomodulin incubation was significantly higher than in the benign ovarian group (p< 0.01). In patients who developed VTE post surgery, higher levels of ETP and peak thrombin (p< 0.01) were found preoperatively compared with patients who did not develop VTE.

Conclusions: Patients with clear cell cancer have increased procoagulant activity as measured by ETP assay. The increased procoagulant activity is likely to contribute to the higher incidence of VTE in these patients. This procoagulant activity may be caused by the increased TF expression by tumour tissue (which we have reported). Following chemotherapy patients have reduced sensitivity to thrombomodulin indicating a defect in the protein C inhibitory pathway. ETP may be a potential marker for VTE in Gynaecology oncology patients post surgery.
Poster Session I

ETP AS A MARKER FOR VENOUS THROMBOEMBOLISM IN GYNAECOLOGICAL CANCER PATIENTS POST SURGERY

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Introduction: Gynaecological cancers increase the risk of venous thromboembolism (VTE). Women having pelvic surgery are routinely given prophylactic low molecular weight heparin (LMWH) post surgery to decrease the VTE risk. Despite this a significant number of women will develop VTE following discharge from hospital.

Aims: The aim of this study was to evaluate the changes in procoagulant activity in women before and after surgery in patients with benign and malignant endometrial and ovarian disease.

Patient and methods: Thrombin generation in platelet-poor plasma was measured using the Calibrated Automated Thrombography in patients with malignant and benign ovarian and endometrial disease; preoperatively, on day 5 post surgery, 2 and 6 weeks post discharge from hospital. Lag time, peak thrombin production, area under the thrombin generation curve (ETP), time to peak (TTP) were determined.

Result: Two weeks post surgery, ETP was higher (p< 0.05) in the malignant compared with the benign group. There was no significant difference between benign and malignant groups in preoperative, day 5 and week 6 samples. In patients who developed VTE post surgery, higher levels of ETP and peak thrombin were found compared with patients in the malignant group who did not develop VTE.

Conclusion: Following cessation of LMWH, patients with gynaecological cancer had increased procoagulant activity compared with those with benign disease. This may be related to the cancer itself or result from the more prolonged and/or extensive surgery performed in cancer patients. ETP may be a potential marker for VTE in Gynaecology oncology patients post surgery.
Poster Session I

KRUKENBERG TUMOURS - A RARE ENTITY: THE OMANI EXPERIENCE

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Objectives: Krukenberg tumours of the ovaries are uncommon. In most cases the primary is in the gastrointestinal tract, the Stomach being the most frequent followed by the colon, breast and appendix. It carries a high mortality rate and to date no curative treatment is available. We report our experience at Sultan Qaboos University Hospital (SQUH), Oman.

Methods: Case notes of all Krukenberg tumours diagnosed between 2006 and 2011 were reviewed.

Results: Seven women were identified out of sixty patients (median age 41; range 18-60). In three, colon cancer was the primary, followed by the stomach in two, lymphoma in one and leukemia in another. Two had mucinous adenocarcinomas of the colon and stomach. Clinical presentation was variable and included backache, abdominal pain, altered bowel habits, rectal bleeding, menstrual irregularity, epistaxis and fever. CA 125 was raised in six and was not checked in one. CEA was only checked in two patients and was elevated. Ascites was present in four cases. In all but one case, the diagnosis of a metastatic Krukenberg tumour was made prior to debulking surgery. Median survival was 4 months (2-24 months). One patient is still alive 14 months after diagnosis.

Conclusions: The diagnosis of Krukenberg tumours requires a high index of suspicion. Out of 60 patients diagnosed to have malignant ovarian masses during the study period, 7 had Krukenberg tumours (8.5%). A national data base register for these cases is crucial.
Poster Session I

A DETAILED STUDY OF PATIENTS AND TUMOR CHARACTERISTICS OF EPITHELIAL OVARIAN CANCER IN SAUDI WOMEN

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Background: The Saudi population is characterized by high parity and inter-marriages that may impact ovarian carcinogenesis. Herein, we analyzed the tumor characteristics and outcomes in Saudi patients with epithelial ovarian cancer (EOC).

Material and methods: EOC patients treated at King Faisal Specialist Hospital during 1995-2007 were identified retrospectively through review of the medical records. Patients/tumor characteristics were collected including: age at diagnosis, marital status, parity, histology, stage, treatment rendered, and follow-up data.

Results: 193 patients with EOC were identified in this cohort. Mean age was 55.1 years, body-mass index (BMI) was 27.2 kg/m². Median parity was 7.0. Only one patient reported family history of cancer (pancreatic cancer in father; 164 women reported negative family history; 27 were not available). Tumor distribution by FIGO stage was: 12 (6.2%) women stage I, 1 (0.5%) stage II, 130 (67.4%) stage III, 39 (20.2 %) stage IV disease, and 11 (5.7%) unknown. Information on residual disease was available on 98 patients only with optimal debulking (< 1 cm) completed on 61 patients. The median PFS from end of chemotherapy to recurrence/progression was 11.2 months (95% CI 8.8-14.3). Tumor histology, size of residual disease, and stage at diagnosis were significant prognostic factors. Age, BMI, tumor histology and grade had no impact on survival.

Conclusion: Patients presenting with advanced-stage disease is higher among Saudis than those reported in global literature. Despite high-intermarriage rates, reported family history for related cancers was quite low in this cohort. Notably, this is the first study evaluating at EOC in Saudi patients.
Poster Session I

MALIGNANT TRANSFORMATION OF A CYSTIC TERATOMA INTO AN ANGIOSARCOMA: A CASE AND REVIEW OF THE TREATMENT LITERATURE

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Introduction: While mature cystic teratomas are the most common ovarian tumors and are usually benign, they carry up to a 2% risk of malignant transformation. An angiosarcoma is a very rare form of this transformation. We present a case of malignant transformation of a mature cystic teratoma into an angiosarcoma and review the literature on treatment options for this aggressive disease.

Case report: A 64-year-old female with acute abdominal pain presented with symptoms and signs suggestive of acute peritonitis. A CT scan showed large abdominal masses invading and perforating the sigmoid colon and terminal ileum. Despite debulking and adjuvant paclitaxel, the patient’s disease rapidly progressed and she died 8 weeks after diagnosis.

Current NCCN guidelines for intra-abdominal soft tissue sarcomas recommend tumor resection with or without preoperative chemotherapy or radiation therapy. For recurrent disease, a combination of surgery, chemotherapy, radiation therapy, and/or supportive care is indicated. Specific chemotherapies suggested for angiosarcomas include paclitaxel, docetaxel, vinorelbine, sorafenib, sunitinib, and bevacizumab or other chemotherapies used for soft tissue sarcomas of the abdomen and extremities. However, angiosarcomas may have a more robust response to paclitaxel.

Conclusion: Angiosarcomas of the ovary are very rare. After debulking, adjuvant paclitaxel is commonly used. The aggressive nature of this cancer warrants exploring the use of the newer anti-angiogenic chemotherapies that may provide longer progression-free survival.
Poster Session I

STUDY OF CA72-4 SERUM LEVEL IN MENOPAUSE WOMEN

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Background: Carbohydrate/cancer Antigen (CA 72-4) implied as a tumor marker in the screening of epithelial ovarian cancer in the some studies. But the results are inconsistent. The aim of this study was to evaluate the clinical usefulness of CA 72-4 as a serum tumor marker for ovarian cancer in menopause patients.

Materials and method: Serum concentrations of CA 72-4 were evaluated in 100 patients with ovarian cancer and 200 menopause healthy volunteers during a 3-year period. CA 72-4 assay was made with ELISA. The data was analyzed by SPSS software using chi-square, T test and Pearson correlation test. We correlated clinico-pathological parameters with serum CA 72-4 levels.

Results: Patients with ovarian cancer had a significantly higher serum CA 72-4 levels. (n=200; 14.6±3.33 U/ml ) compared with controls with no ovarian pathology (n=100;0.52 ±1.2U/ml; P< 0.0001). Parity, infertility, history of oral contraceptive usage, or hormone replacement therapy was not significant influences on CA72-4 level when analysis of covariance was performed. Age was weakly correlated with CA72-4 level in the study groups but this is not statistically significant (r: 0.023; P: .751 in cancerous group, r:0.021;P:.701 in healthy group).

Conclusion: CA 72-4 level of patients with ovarian cancer obviously changes; it is helpful to improve diagnostic rate of ovarian cancer. We have also shown that age might influence on the level of tumor marker but further longitudinal studies are needed to investigate it.
Poster Session I

RISK FACTORS ASSOCIATED WITH NON-HOME DISCHARGE AND INCREASED LENGTH OF STAY IN EPITHELIAL OVARIAN CANCER

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Background: Identification of preoperative and intraoperative factors predictive of non-home discharge and increased length of stay (LOS) after epithelial ovarian cancer (EOC) surgery may help in preoperative counseling and optimization of discharge planning.

Objectives: To determine the association between preoperative/intraoperative factors and non-home discharge and increased LOS.

Methods: Patients who underwent EOC surgery between 1/2/03-12/29/08 were included. Demographic, preoperative and intraoperative factors were retrospectively abstracted. Logistic and linear regression models were fit to identify factors associated with non-home discharge and ln(LOS), respectively. Multivariable models were developed using stepwise and backward variable selection.

Results: Of 587 patients evaluated, 75 (12.8%) were not discharged home (61 nursing home, 1 rehab, 1 hospice, 12 in-hospital deaths). In multivariable analyses, patients with advanced age (p<0.001), poorer ECOG performance status (p<0.001), cardiac disease (p=0.01), higher CA-125 (p=0.03), omental disease (p=0.01), and advanced stage (p=0.01) were less likely to be discharged home. Factors associated with increased LOS are shown in table 1.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASA level (≥3 vs. &lt;3)</td>
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</tr>
<tr>
<td>Preoperative CA-125</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FIGO stage (III and IV vs. I/II)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estimated blood loss</td>
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</tr>
<tr>
<td>Operative time</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Surgical complexity score (intermediate and high vs. low)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Residual disease (any measurable vs. microscopic)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

[Table 1]

Conclusions: There are preoperative and intraoperative factors associated with non-home dismissal and increased LOS. Future development of a risk-scoring system is warranted.
Poster Session I

DOES MODALITY OF ADJUVANT CHEMOTHERAPY ADMINISTRATION AFTER INTERVAL SURGICAL DEBULKING MATTER IN EPITHELIAL OVARIAN CANCER?

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Objectives: To study the role of intraperitoneal (IP) chemotherapy after neoadjuvant chemotherapy and interval surgical debulking.

Method: All neoadjuvant treated epithelial ovarian cancer patients were retrospectively reviewed from 2007-9. Demographics, disease related and survival outcome data were abstracted from electronic medical records. Chi Square statistics were used for categorical variables. Cox regression was used to model progression free survival adjusting for age, residual status, and use of IP chemotherapy. Log rank statistic was used to compare survivals between IP and IV treated patients after surgery. All p values less than 0.05 were considered to be statistical significant.

Results: 65 patients were reviewed. Median age was 63yo. The majority had stage 3/4 disease with serous histology. Optimal residual was achieved in 52% of patients. Half of these patients went on to be treated with IP chemotherapy. Median follow up was 26.2 months. Fifty one patients had progressed with the median progression free survival (PFS) of 14.5 months. Use of IP chemotherapy post interval debulking surgery was not significantly associated with PFS (HR 0.82 95% CI 0.31-2.22 p=0.70). Estimated median overall survival was 37.8 mos (95% CI 29.9-45.7) in IV treated only versus 48.1 mos (95% CI 37.9-58.3) in IP treated patients (p=0.162).

Conclusion: IP chemotherapy was not statistically significant associated with survivals in neoadjuvant treated ovarian cancer in our early experience. The role of IP chemotherapy after neoadjuvant chemotherapy need to be further defined pending on the final mature result of OV 21 study currently accrual patients.
Poster Session I

DOES SYMPTOMATIC RECURRENCE INFLUENCE PROGNOSIS IN EPITHELIAL OVARIAN CANCER?

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Objectives: The prognostic significance of symptomatic recurrence has been poorly studied. We compare survival outcomes in patients with symptomatic recurrences to asymptomatic recurrences diagnosed by CA125 / routine imaging after primary therapy.

Method: All epithelial ovarian cancer patients with first progression were retrospectively reviewed from 2007-9. Demographics, disease related and survival outcome data were abstracted from electronic medical records. Chi Square statistics were used for categorical variables. Cox regression was used to model overall survival adjusting for age, residual disease status, adjuvant therapy use, and presentation at time of first recurrence after primary treatment. Log rank statistic was used to compare survivals. All p values less than 0.05 were considered to be statistical significant.

Results: 100 patients with first recurrence were reviewed. Median age was 62yo. The majority had stage 3/4 disease with 70% having serous histology. First recurrence was diagnosed by CA125 elevation, clinical symptoms, and routine imaging in 60, 9, and 31 patients respectively. Median follow up was 28.2 months. The median progression free survival (PFS) was 16 months. Symptomatic recurrence was not significantly predictive of overall survival compared to asymptomatic recurrence (p=0.82). Estimated median overall survival was 43.8 mos (95% CI 38.4-49.3) in asymptomatic versus 43.7 mos (95% CI 25.2-62.3) in patients with symptomatic clinical recurrences (p=0.99). Use of adjuvant intraperitoneal chemotherapy showed a trend towards improved overall survival (HR 0.47 95% CI 0.19-1.13 p=0.09).

Conclusion: Symptomatic recurrence at time of first progression is not associated with worsened overall survival.
Poster Session I

THE EFFECTS OF ANEMIA AND BLOOD TRANSFUSION ON PATIENTS WITH STAGE III-IV OVARIAN CANCER
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Objectives: The objective of this study was to examine the overall and recurrence free survival in patients with advanced ovarian cancer based on hemoglobin and blood transfusion status.

Methods: A retrospective chart review was performed at the Tom Baker Cancer Centre between 2003 and 2007 on patients with pathologically confirmed stage 3 or 4 ovarian, fallopian tube or primary peritoneal cancers. Data was collected on date of diagnosis, recurrence and death, stage, grade, age, type of surgery, optimal debulking, estimated blood loss, hemoglobin (nadir and average levels) and number of blood transfusions.

Results: 216 patients were included in the final analysis. In the peri-chemotherapy, peri-operative and total time frames: 88%, 81% and 95% of patients were anemic, and 9%, 22% and 26% of the patients had severe anemia. After adjusting for age, cancer stage, and optimal debulking status, the peri-chemotherapy hemoglobin level as a continuous variable was weakly associated with recurrence-free survival (adjusted hazard ratio (AHR)=0.98 and p=0.03), and as a categorical variable with both recurrence-free survival (AHR=2.49; p=0.003) and overall survival (AHR=1.91; p=0.02). Total number of blood transfusion was also weakly associated with poor recurrence-free survival (AHR=1.06; p=0.03).

Conclusion: Our study is the first retrospective analysis of the effects of anemia and blood transfusion on ovarian cancer. The rates of anemia in chemotherapy patients are higher than previously reported in the oncology literature. In contrast to colorectal cancer, there is no association of anemia or blood transfusion in the peri-operative period to recurrence-free or overall survival. Although maintaining average hemoglobin above 80 g/L during chemotherapy portends an improved overall survival, blood transfusion does not seem to have any effect. The role of transfusion should therefore be limited to symptomatic patients while giving one unit at a time. Further prospective studies will be needed to confirm these results.
Poster Session I

THE DIAGNOSTIC UTILITY OF P53/P16 TO DISTINGUISH HIGH-GRADe FROM LOW-GRADe SEROUS CARCINOMAS


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Introduction: Low-grade serous carcinomas (LGSC) are known to be less responsive to standard platinum chemotherapy compared to high-grade serous carcinomas (HGSC). The discrimination between LGSC and HGSC can be challenging on small tissue samples.

Objective: To test the discriminatory power of p53 and p16 expression assessed by immunohistochemistry between HGSC and LGSC.

Material and methods: Tissue microarrays containing 61 HGSC and 24 LGSC, confirmed by histopathological review, were constructed. P53 and p16 stains were done on the Leica Bond platform (DO7 and E6H4 antibody clones in 1:5000 and 1:24 dilution). P53 was scored as complete absent, wild type pattern and over-expression (> 60%), and p16 as negative/patchy (< 90% of tumor) and block expression (> 90% of tumor). Data from an independent set of 131 cases was used for validation.

Results: In the training set, the sensitivity of p53 wild type for LGSC was 96% and the specificity 88%. The sensitivity of patchy p16 expression for LGSC was 91%, and specificity is 69%. The combination of the two markers had a sensitivity of 83%/87%, a specificity of 94/95%, a positive predictive value of 41%/87% and a negative predictive value is 99%/95%, respectively for training and expansion set.

Conclusion: The combination of p53 /p16 has a negative predictive value of 95%-99% depending on LGSC prevalence. These markers can therefore be used on small biopsies/cellblocks to refute a diagnosis of LGSC. These findings may guide clinical practice to determine patients that would benefit from upfront surgery (LGSC) versus combined chemotherapy/surgical (HGSC) approach.
Poster Session I

MODEL SYSTEMS FOR TYPE-SPECIFIC OVARIAN THERAPEUTIC RESEARCH: CLEAR CELL CARCINOMA OF THE OVARY

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Introduction: Ovarian carcinomas are a diverse set of at least five distinct diseases including High-grade serous, Low-grade serous, Clear cell, Endometrioid, and Mucinous types. Biomarker and molecular studies can segregate each type and provide a more relevant basis for grouping and treating this family of tumours rather than presumed site of origin. Although molecular characteristics are becoming the new standard for clinical pathology, development of type-specific therapies is hampered by continued use of inappropriate cell line model systems that do not stratify ovarian cancer disease types.

Methods: We focused on identification of bona-fide clear cell carcinoma cell lines, and classified 21 common “ovarian cancer” lines into histotypes using immunohistochemistry (IHC), and sequencing of commonly altered cancer genes.

Results: Most of the described clear cell lines retain a representative immuno-profile and mutations consistent with their origin. Assignment of ovarian cancer type can be done with confidence and suggest some cancer cell lines are mis-used. One example is A2780, commonly used as high-grade serous cancer, which is highly likely to be endometrioid type. A more detailed compendium of data characterizing clear cell carcinoma cell lines, including copy number and transcriptome analysis, is also presented.

Conclusions: Immuno-profiling and mutation testing of genes like ARID1A and p53 serve well for establishing ovarian cancer histotypes in cell lines. As biomarkers and molecular features of ovarian carcinomas are well established, a process of type-specific model evaluation should become the new standard in executing ovarian cancer research.
Upper panels shows partial immuno-profile and lower panel show DNA copy number (red for gain, blue for loss on inner ring) and genomic re-arrangement (green lines in centre) in a genomic circos plot for a bonafide clear cell line (TOV21G)

[Figure 1]
**Poster Session I**

**NEOADJUVANT CHEMOTHERAPY (NACT) AND FERTILITY PRESERVING SURGERY IN ADVANCED MALIGNANT OVARIAN GERM CELL TUMORS**

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**Introduction:** Malignant ovarian germ cell tumors (MOGCT) represent only 2-5% of the ovarian malignancies. But their peak incidence is in young women or adolescent girls and account for 58% of all ovarian tumors in women younger than the age of 20. In India, where arranged marriages are quite common, the issue of surgical scar and future fertility is of great concern to parents.

**Aim:** To evaluate role of NACT followed by fertility preserving surgery in patients with MOGCT (Stage Ic or more).

**Methods:** This was a prospective study carried out from September 2004 till December 2011 at Amrita Institute of Medical Sciences, Kerala, India. The diagnosis and stage were established with the help of Biopsy/Cytology, Tumor markers and Imaging. All patients with Stage Ic and above were offered the options of either primary surgery or NACT.

**Results:** We had 28 patients with MOGCT during this period and 9 were selected for NACT. Mean age of this group was 22yrs. Two patients were stage IV, five stage IIIC and two stage Ic. NACT with Bleomycin, Etoposide and Cisplatin was given for all. Fertility preserving surgery was done in eight patients. Eight patients had complete pathological remission. After a mean follow up of 39 months all patients are alive and disease free. All patients who underwent fertility preserving surgery resumed normal menstrual cycles and two became pregnant after the completion of treatment.

**Conclusion:** NACT causes pathological CR in most and reduces the surgical morbidity. Since MOGCT affects young, mostly unmarried people, in the Indian cultural context, where arranged marriages are more the norm than exception, a long surgical scar is a matter of great concern as it does affect the future marriage prospects. NACT paves the way for a smaller surgical scar and even for robotic or laparoscopic surgery.
Poster Session I

THE RISING RATE OF CA125 AFTER THE FIRST ADMINISTRATION PREDICTED THE RESPONSE OF PEGYLATED LIPOSOMAL DOXORUBICIN (PLD)

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Objectives: To examine the correlation between the rising rate of CA125 and response rate in patients treated with PLD for recurrent ovarian carcinomas (ROC).

Patients and methods: Between 2008 and 2012, seventeen patients were treated with PLD at a dose of 50 mg/m2 q4weeks for ROC at our hospital. CA125 measurement was performed each cycle of administration. The evaluation of tumor response by RECIST was carried out after two or three cycles. CA125 before the first administration was defined as the baseline, and we calculated the rising rate from the baseline after each cycle.

Results: The overall response rate defined as complete remission (CR) and partial response (PR) was 12%. The clinical benefit rate (CBR) defined as CR, PR, and stable disease (SD) was 47%. The CA 125 transiently increased before the two cycles in 14/17 (82%) patients. The average rising rate after the first cycle in patients with CBR were lower than those with progressive diseases (PD) (p<0.01). The cut-off value of the rising rate after the first cycle with a sensitivity of 67% and specificity of 88% was 150%.

Conclusion: The transient rise of CA125 after the first administration of PLD was frequently discovered but the rising rate of CA125 in most patients with PD exceeded 150%. The rising rate of CA125 after the first administration might be the predictive sign of non-responder.
Primary Malignant Mixed Müllerian Tumor of the Fimbriated End of the Fallopian Tube Causing Hematosalpinx and Hematometra

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Malignant mixed müllerian tumor (MMMT) of the fallopian tubes is one of the rarest tumors of the reproductive tract. Furthermore, the localisation of the fimbriated end even less has been reported. Herein we report a case of primary MMMT of the fallopian tube causing hematosalpinx and hematometra in a 64 year old woman with a complaints of watery/bloody vaginal discharge and lower quadrant abdominal pain. Imaging methods determined 14 cm length tubal mass and at distal end of this structure, approximately 6-cm heterogeneous solid mass determined. The patient underwent bilateral salpingo-oophorectomy, hysterectomy, omentectomy and pelvic and paraaortic lymphadenectomy. After the pathologic analysis of the material, the patient was categorized as FIGO Stage IIc. She received six cycles of carboplatin and paclitaxel at 21day intervals. She is now doing well without recurrence of disease. The conditions that accompanying hematosalpinx and hematometra, a rare malignities of tuba should be kept in mind.
Poster Session I

EFFICACY OF GYNECOLOGICAL SURVEILLANCE ON OVARIAN CANCER IN WOMEN WITH LYNCH SYNDROME

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Introduction: Approximately, one percent of all epithelial ovarian cancers is related to Lynch syndrome. Gynecological surveillance in BRCA mutation carriers and general population is not effective. The aim of this study was to evaluate the efficacy of gynecological surveillance with regard to ovarian cancer in women with Lynch syndrome.

Methods: Women with Lynch syndrome or meeting the Amsterdam II criteria were included. Annual gynecological surveillance was performed with transvaginal ultrasound (TVU) and Ca125 assessment starting at the age of 30.

Results: In 140 women, 553 surveillance visits (530 follow-up years) were performed, and 76 additional interval visits due to abnormal findings at surveillance and/or complaints. In 65% of these visits, women were at least 40 years. 123 women (88.5%) had a mutation in a mismatch repair gen. Median follow-up was 4.0 years (range 0-15.4). Thirteen women had surgery for abnormalities in ovarian surveillance (pelvic examination, Ca125 assessment and/or TVU) resulting in one primary ovarian cancer FIGO stage IIIc diagnosed in a 49-year-old woman without complaints and normal TVU, but a high Ca125 at primary visit. Abnormal pelvic examination revealed one asymptomatic mature teratoma. Two borderline malignancies were found by elevated Ca125, either one had an enlarged ovary on TVU. Nine women underwent an unnecessary surgical procedure.

Conclusions: Gynecological surveillance on ovarian cancer in Lynch syndrome seems not to be effective. One ovarian cancer stage IIIc was detected at primary visit. Two borderline malignancies were found, but a relationship with Lynch syndrome is not known, so probably these tumors were coincidental.
Poster Session I

YOUNG WOMEN ≤ 40 YEARS WITH EPITHELIAL OVARIAN CANCER REFERRED FOR GENETIC TESTING: NO INCREASED RISK ON BRCA MUTATION

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Introduction: Cancer at young age may point to a hereditary basis. Epithelial ovarian cancer (EOC) in women ≤ 40 years is rare. The impact of the diagnosis at this age justifies referral for genetic testing. The aim of this study was to evaluate the risk of identifying BRCA mutations and clinic pathological features in young women with EOC.

Methods: All women ≤ 40 years with EOC referred to the Department of Clinical Genetics for BRCA mutation analysis between 1996 and 2011 were included. Clinic pathological features and family history were compared between BRCA carriers and non-carriers.

Results: Of 50 women ≤ 40 years with EOC, nine women (18%) had a BRCA mutation. Median age of diagnosis was significantly lower in non-carriers compared to BRCA carriers (30 versus 38 years). In women under 36 years, no mutations were found. Among BRCA carriers, 67% had serous tumors, 78% stage III/IV and 100% moderately to poor differentiated tumors, compared to respectively 54%, 46% and 49% in non-carriers. A first degree family history of breast and/or ovarian cancer was reported in 67% and 7% of relatives of carriers and non-carriers, respectively.

Conclusions: Young women with EOC will be referred for genetic counseling for a low change identifying a BRCA mutation, because of the impact of BRCA on patients and their family members. Gynecologists have to reassure these young women and their relatives with respect to the risk of an underlying hereditary basis, especially when diagnosed before mid-thirties and a negative first degree family history.
Detecting Recurrent Epithelial Ovarian Cancer in Tehran, Iran

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Objective: We evaluated the role of the Surveillance in the detection of recurrence after initial therapy for epithelial ovarian cancer.

Material and methods: From December 1995 to September 2005, 286 patients underwent surgery for invasive epithelial ovarian cancer at Gynecologic Oncology Department, Vali Asr Hospital, Tehran, Iran. Among these patients, 69 were available for the retrospective analysis. Follow-up examinations included clinical examination, serum tumor marker assay, transvaginal and transabdominal sonography and CT scan/MRI. Data from the patients' files and pathologic reports were analyzed. The disease-free interval was calculated from the completion of their primary chemotherapy, provided their tumor markers had returned to normal. Recurrence was diagnosed when at least one of the following criteria was abnormal: symptoms, physical examination or elevated serum CA125 levels.

Result: Forty-one cases of invasive epithelial ovarian cancer were identified who had tumor recurrence after a disease-free interval. The mean age was 49.8 (19-82) years. The median disease-free interval was 11.4 months, and 73.7% of the patients had FIGO Stage III/IV disease. At the time of diagnosis the recurrence 70.7% of patients had no symptoms. Of all recurrence, 19.5% only picked up by physical examination. Gross recurrent disease confined to the intraabdominal or pelvic site.

Conclusion: Documentation of early tumor recurrence should allow more prompt treatment of these patients at a time when tumor cell numbers are low, thereby increasing duration of survival.
Poster Session I

ENDOMETRIOSIS RELATED OVARIAN CARCINOMAS: A CLINIC-PATHOLOGIC ANALYSIS OF 43 PATIENTS

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Objective: The relationship between endometriosis and ovarian carcinomas has been investigating for decades starting from Sampson 1925. The aim of this study to identify epithelial ovarian cancers derived from endometriotic foci.

Material and methods: We retrospectively analysed 43 patients with ovarian carcinoma arising from endometriotic cyst. Four hundred Patients with ovarian carcinoma undergone surgery between the years 2007-2012 in our institution. Pathology reports are re-evaluated by co-author pathologist and reported as arising from endometriotic cyst. Statistical analyses are done by using spss 16.

Results: The number of endometriosis associated ovarian carcinoma is 43 and 10.7 % (43/400) of all epithelial ovarian carcinomas. The mean age was 47.2 (range 28-75 years). The most common histologic subtypes were: endometrioid 37.2% (16/43) and clear cell 30.2 % (13/43). Surgical staging was based on FIGO staging system and the leading stages were stage 1a 41.8 % (18/43) and stage 1c 20.9 % (9/43). Mean follow up time 24 months (range 2-58 months) 2 patients died during this follow up time.

Conclusion: There is a link between endometriosis and epithelial ovarian carcinomas this association is 10.7 % in our study and it was 14.5 % in a Japan study (H. Jimbo and colleagues). Further studies are needed to reach a clear conclusion especially based on monoclonal genetics.
Poster Session I

SINGLE INSTITUTE EXPERIENCE OF REPEATED CYTOREDUCTIVE SURGERIES IN OVARIAN CANCER; SURVIVAL AND MORBIDITY

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Background: Secondary cytoreductive surgery and also tertiary were performed in selected patients for many years. Survival benefit was shown in the published studies.

Objective: Aim of the study was to evaluate survival and the toxicity after secondary and tertiary surgery in this cohort.

Material and methods: In this study 106 patients were subjected to secondat cytoreduction in baskent university hospital between 1/2/2007 and 1/2/2012. Median follow up time were 40 months (4-130 months range). Stastical analyses were done by using SPSS 17.0 statistic programme. To detect survival rates Kaplan-Meier survival analysis is used, and comparisons are made by log-rank tests. For all analysis, significance value is defined as ‘p<0.05’.

Results: Median overall survival were found 56.0±5.8 months; 59.0±7.1 months and 59.0±8.6 months respectively for secondary, tertiary and quarternary cytoreductive procedures. Grade 3 and grade 4 toxicity were found at %6.4; %4.7; %19.1; %20 of patients respectively after primary, secondary, tertiary and quarternary cytoreductive procedures. Details about this cohort will be given at poster presentation.

Conclusion: Cytoreductive surgery, in selected ovarian carcinoma patients, improves survival benefits and has tolerable toxicity.
Poster Session I

RARE BUT REAL: EPITHELIAL OVARIAN CANCER IN YOUNG WOMEN

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Aims: To review data of young aged women with epithelial ovarian cancer (EOC), all of which were diagnosed and treated in the gynecologic oncology department of Zekai Tahir Burak Women’s Health and Research Hospital, Ankara, Turkey.

Methods: Hospital cancer registry database was reviewed EOC cases recorded between January 2007 and December 2011. Patients who were ≤30 years of age at the time of diagnosis were included in the study.

Results: A total of 320 ovarian cancer cases were performed in our institution during a five-year period. Among these, 249(78%) were EOC. Seventeen (6.8%) of EOC cases who were aged ≤30 years at the time of diagnosis were included in analysis. Mean patient age was 28.2±1.6 years. Six cases(35.3%) had mucinous, 5 cases(29.4%) had serous, 3 cases(17.6%) had endometrioid, 2 cases(11.8%) had clear cell adenocarcinoma. One case(5.9%) was diagnosed with serous adenocarcinofibroma. Five cases(29.4%) had FIGO stage IA, 2 cases(11.7%) had stage IB, 3 cases(17.6%) had stage IC, 2 cases(11.7%) had stage II and 5 cases(29.4%) had stage IIIC disease. Complete surgical staging including hysterectomy was performed in 12 cases(70.6%), whereas fertility sparing surgery was accomplished in 5 cases(29.4%). All of the patients received adjuvant chemotherapy (paclitaxel and carboplatin).

Conclusions: Although generally considered a disease of postmenopausal period, EOC is rarely encountered in young women of reproductive age group. Future fertility is commonly a concern in these cases. Fertility preservation may be considered in FIGO stageIA tumors; however, removal of the uterus and the remaining ovary is recommended after completion of childbearing.
Poster Session I

CLINICAL OUTCOME OF WOMAN WITH GYNECOLOGIC TUMORS TREATED WITH SUGARBAKER PROCEDURE IN COLOMBIA

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Background: Sugarbaker procedure (SP) consists on radical peritonectomy plus hyperthermic intraperitoneal chemotherapy (HIPEC). It is done in well selected gynecologic malignancies.

Objective: To characterize a case-series of patients with gynecologic tumors treated with SP in Colombia.

Results: Patients treated with SP have been 42, 19% had gynecologic malignancies. Median age was 50.2 years (26-64). 75% of diagnosis comprises mucinous ovarian/serous carcinoma; there was a well-differentiated angiosarcoma and one carsinosarcoma. CT-scans described peritoneal nodules (50%) and ascitis (37.5%). Previous administration of platinum-based-chemotherapy was given with a median of 6 cycles (4-9). Median CA-125 was 66.1 (9-816). 75% had previous hysterectomy and salpingo-oophorectomy. The SP included pelvic peritonectomy in all cases and omentectomy in 87.5%. Half of patients required any intestinal resection. HIPEC was administrated with DDP+doxorubicin (75%) and paclitaxel (25%).

Median duration of procedure was 12.2 hours (7.4-16.0). Median days of UCI=6 (2-12) and median days of hospitalization=17.5 (10-36). Hematologic toxicity was seen in 50%. 37% showed grade 2 gastrointestinal toxicity. Nephrotoxicity, pancreatitis and fistula was seen each one in 25% of cases.

50% of patients recurred with a median Recurrence-Free Survival (RFS) of 21 months (10,2-31,7). All patients recurred when procedure was made after recurrence of previous procedures (median=13months) or as first line of treatment. 25% of recurrences seen when procedure was done in consolidation (after platinum-based chemotherapy and resection). No one patient has died at the time of analysis.

Conclusions: Recurrence-Free Survival was better when procedure was done after platinum-based chemotherapy and previous debulking, in consolidation. Procedure has demonstrated safety and efficacy in Colombia.
Poster Session I

PHASE II TRIAL OF WEEKLY TRABECTEDIN PLUS WEEKLY PEGYLATED LIPOSOMAL DOXORUBICIN FOR TREATMENT OF ADVANCED, PERSISTENT OR RECURRENT OVARIAN CARCINOMA

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Objective: The objective of this study was to determine safety, feasibility and efficacy of weekly Trabectedin (T) 0.4 mg/mq IV in combination with weekly Pegylated Liposomal Doxorubicin (PLD) 10 mg/mq (p1,8,15 q28) in patients with recurrent ovarian cancer.

Patients and methods: We carried out a single Institute Phase II trial in patients with advanced recurrent ovarian cancer. Eligibility criteria included: age 18-75; recurrent and measurable disease; acceptable organ function; normal blood chemistry parameters; ≤3 prior regimens; ECOG performance status 0-1; life expectancy > 3 months; signed informed consent. Trabectedin (0.4 mg/mq) was administered weekly via a central line, after premedication with dexamethasone, as a 3-h infusion weekly for 3 weeks followed by weekly infusion of Caelyx 10 mg/mq. Therapy continued until disease progression, unacceptable toxicity or patient refusal.

Results: Between March 2010 and February 2012, 22 patients were recruited; median age was 54 years (range: 39-74). The median number of cycles was 5 (107 total cycles, range 2-11). In 5 patients (23%) an objective response rate with measurable disease was achieved. The median progression-free survival was 4.8 months. No unexpected toxicities were found. The most frequent treatment-related grade 3/4 adverse events included neutropenia (27%), thrombocytopenia (9%), nausea/vomiting (13%), fatigue (13%) and reversible AST/ALT elevation (23%). No drug related cardiotoxicity was observed. There were no treatment-related deaths nor cases of liver failure.

Conclusions: Weekly administration of T and PLD is a safe and feasible therapeutic option for recurrent ovarian carcinoma. Further studies are needed in order to confirm these data.
Poster Session I

OVARIAN CANCER IN BRCA1 AND BRCA2 GENE MUTATION CARRIERS: ANALYSIS OF PROGNOSTIC FACTORS AND SURVIVAL

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Background and aims: To compare clinical-pathological characteristics and outcome of hereditary and sporadic ovarian cancer.

Methods: Twenty-four ovarian cancer patients treated between January 2000 and June 2011 who tested positive for BRCA1/2 mutation (BRCA+) and a control group of 64 patients untested, but without personal history of breast cancer and no family history of breast/ovarian cancer (controls) were enrolled. Main clinical-pathological characteristics, surgical outcome, overall (OS) and disease free survival (DFS) were compared between the two groups.

Results: The serous papillary histotype was not-significantly more represented in BRCA+ vs controls (70.8% vs. 53.1%; p=0.31). Controls were diagnosed at a more advanced stage (56.2% stage III and 20.3% stage IV) as compared to BRCA+ (45.8% stage III and 8.3% stage IV; p=0.01). Radical primary surgery was performed in 70% of women in both groups; however, suboptimal cytoreduction (residual tumor >1 cm) was obtained more frequently in controls as compared to BRCA+ (11.3% vs 5.8%; p=0.00). Survival was significantly better for BRCA+ (p=0.00), with 50% of controls relapsing within 2 years from surgery.

Conclusion: BRCA carriers develop predominantly serous papillary ovarian cancers and carry a better prognosis than controls. Higher chemosensitivity of BRCA+ tumors has been reported, but lower stage at diagnosis and higher rate of optimal cytoreduction may also exert a positive influence on their final outcome.
Poster Session I

THE HISTOLOGICAL PATTERN OF OVARIAN TUMOR IN PATIENTS WITH OVARIAN TUMOR REFERRED TO YAHYANEJAD HOSPITAL IN NORTH OF IRAN, BABOL

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Introduction: Ovarian cancer has a large variety due to histology structure which this difference could be due to different communities. The aim of this study was to evaluate the frequency of ovarian tumors in our area.

Materials and methods: This cross-sectional study was performed on 150 women with ovarian tumor referred to Yahyanejad Hospital in 2007 to 2009 in North of Iran.

Results: From 127 patients with ovarian masse, 84 cases (7%) were benign, 23 cases (15.3%) were borderline and malignant. Histological type of benign ovarian tumor included simple cyst mucinous 6 (4%), mucinous cyst adenoma 14 (9.3%), and serous cyst adenoma 1 (0.7%). Dermoid cyst 29 (19.3%). Endometrioma 37 (24.7%), simple cyst follicular 10 (6.7%), hemorrhagic cyst 10 (6.7%), corpus luteum cyst 18 (12%), and inclusion cyst 2 (2%). Histological type of borderline tumors was reported serous adenocarcinoma 2 (1.3%), mucinous adenocarcinoma 3 (2%). Histological type of malignant tumor included: adenocarcinoma 1 (0.7%), clear cell adenocarcinoma 1 (0.7%), adenocarcinoma mucinous 2 (1.3%), and serous papillary carcinoma 9 (6%). Disgerminoma 1 (0.7%, and 2 (1.3%) granulosa cell carcinoma. Two cases of metastatic tumors to the ovary was reported.

Conclusions: In this study, endometrioma was the most common ovarian tumors. Serous papillary carcinoma was most common among the malignant tumors.
Poster Session I

HE4 AND CA125: PREDICTIVE BIOMARKERS FOR SURGICAL-OUTCOME AND PROGRESSION-FREE (PFS) AND OVERALL-SURVIVAL (OS) IN PRIMARY EPITHELIAL OVARIAN CANCER (PEOC)

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Optimal surgical cytoreduction and response to platinum-based chemotherapy remain the cornerstones of therapeutic management in pEOC. This study analyzes the predictive and prognostic role of HE4 and CA125 in pEOC at diagnosis and during subsequent follow-up.

Methods: Blood samples from 275 pEOC patients at time of diagnosis and 6 months after end of 1st-line chemotherapy were analysed. Among inclusion criteria radical cytoreductive-surgery and platinum-based chemotherapy were considered.

Results: Within OVCAD-European study, complete cytoreduction with no residual tumor mass (RTM) was obtained in 69.9% patients. HE4 and CA125 at diagnosis correlated with RTM, p = 0.002 and p=0.002, respectively. The sensitivity and specificity of combinative use of both biomarkers in predicting RTM was 64.8% and 73.5%, respectively. Patients having over-expression of both biomarkers had a 6.1 higher risk for RTM (p< 0.001, OR:6.107, 95%CI 2.41-15.46). Platinum-resistance was more likely when both biomarkers were over-expressed (p=0.028, OR= 3.1, 95%CI 1.13-8.46). Elevated biomarkers during follow up predicted recurrence (sensitivity 90% and specificity 71% for CA125 ≥55U/ml; sensitivity 72.7% and specificity 81.4% for HE4 ≥150pM). Elevated CA125 and HE4 was associated with significantly poorer PFS (p< 0.001, HR 9.6, 95%CI 3.93-23.44 with one elevated biomarker, and HR=50.52, 95%CI 14.44-176.78, with both elevated biomarkers) and OS (p< 0.001, HR=7.42 95%CI 1.43-38.42 with one elevated biomarker and HR=28.38 95%CI 6.50-123.97 with both elevated biomarkers).

Conclusions: The combinative use of both biomarkers has significant value in predicting RTM in pEOC. Elevated plasma levels 6 months after 1st-line chemotherapy significantly correlate with OS and PFS in platinum-sensitive patients.
Poster Session I

INTERVAL (IDS) VERSUS PRIMARY TUMOR DEBULKING SURGERY (PDS) IN ADVANCED OVARIAN CANCER (AOC): RESULTS FROM EUROPEAN OVCAD STUDY

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Aim of present study was to evaluated differences in outcome of AOC-patients after PDS versus IDS based on a prospectively assessed multicenter data set.

Methods: Within OVCAD prospective European study, 256 AOC (FIGO-stage III/IV) patients were included. Patients underwent surgery in five comprehensive OC centres across different European countries. All patients treated between 02/2005 and 12/2008 for primary AOC were included. Clinical data were documented using an online data-base. Overall (OS) and progression-free survival (PFS) were calculated by Kaplan-Meier-curves.

Results: Fifty patients (19.5%) underwent IDS and 206 patients (80.5%) PDS. Despite non-randomized setting both groups were well balanced in terms of FIGO-stage, grading, histological subtype and presence of ascites. Different selection criteria were however present for each center. PDS patients presented significantly higher rates of intestinal resection (44.2% vs.24%; p=0.01) and lymphonodectomy compared to IDS ones (72.3%vs.48%; p=0.001), by equivalent complete tumor resection rates (67.5% vs.68%; p=0.82). Platinum-response was significantly higher in PDS vs. IDS patients (80.6% vs. 54%; p< 0.001). 3-years OS was with 66.7% (95%CI: 60.2-73.2%) significantly better in PDS- versus 48.3% (95%CI: 34.2-62.5%) in IDS patients (p< 0.001). Also 2-years PFS was with 31.9% (95%CI:24.8-39.1%) significantly higher in PDS- vs. 11.4% (95%CI: 0.9-22%) in IDS-patients (p< 0.001). In multivariate analysis PDS was of prognostic significance for platinum response. In addition, multivariate analysis identified PDS and no residual tumor to positively and ascites to negatively affect OS and PFS.

Conclusions: In our non-randomized study PDS was associated with better outcome compared to IDS in comprehensive centers.
Poster Session I

UTILITY OF A GYNECOLOGIC DIAGNOSTIC ASSESSMENT UNIT IN THE MANAGEMENT OF PATIENTS WITH ADNEXAL MASSES

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Objective: To evaluate the efficacy in triaging gynaecology patients referred with adnexal masses incorporating a formal Gynecologic Diagnostic Assessment Unit (DAU).

Methods: A DAU has been established at the Ottawa hospital using an accepted protocol incorporating a Risk of Malignancy Index (RMI) score. Patients were triaged to general gynecologists or gyn-oncologists for subsequent management based on the DAU assessment. Patient demographics and pathologic outcomes were abstracted from medical records. The associations between categorical variables were assessed by Chi Squared tests. Logistic regression models were built to evaluate the predictive value of RMI score, menopausal status, and CA125 on final histologic diagnosis.

Results: 173 patients were evaluated from February 2010 to July 2011. We observe a significant association between cancer diagnosis and surgical treatment by a gynecologic oncologist (Chi Squared >18, p< 0.001). Of the 70 cancer patients triaged by the DAU to a subspecialty service, 63 (90 %) were operated on by Gyn Oncologists. Of the 33 patients who were referred back to general gynecologists and surgically evaluated, 26 had final benign pathology (79%).

Logistic regression models predicting malignancy in this data produced an odds ratio of 8.6 (95% CI of 3.34-22.31, p< 0.001) for abnormal CA125, and 5.62 (95% CI of 1.87-16.83 p=0.002) for presentation of 2 or more US abnormalities. In addition, abnormal RMI score of >200 supported an odds ratio of 14.51 (95% CI 5.46-38.50 p< 0.001).

Conclusion: Our DAU was effective in triaging most patients with a malignant diagnosis to be managed by gynecologic oncologists.
Poster Session I

THE RELATIVE FREQUENCY AND HISTOPATHOLOGICAL PATTERN OF OVARIAN MASSES: A UNICENTRIC STUDY OF 212 CASES OF OVARIAN MASS

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Background: Ovarian tumors are one of the major causes of gynecological problems in females and present marked variation in their histological types. Relative frequency of these lesions is different for western and Asian countries. This study was designed to find out frequency of various histological patterns of ovarian tumors in patients attending Pathology Department of a teaching institute in Lahore.

Material and methods: A retrospective study was conducted on 212 cases of ovarian masses, reported from January 2007 to December 2010.

Results: Mean age of the subjects was 35.6 years, ranging from 4 to 80 years. Out of total 212 cases of ovarian masses, 85 (40.09 %) were non-neoplastic and 127 (59.91%) were neoplastic. Among neoplastic lesions, 36.67% (82/127) were benign and 20.75% (45/127) were malignant. The commonest non-neoplastic lesion was luteal cyst (38/86) followed by simple serous cyst (30/86). The commonest benign tumor was dermoid cyst (31/82) followed by serous cystadenoms (20/82). The commonest malignant tumour was serous cystadenocarcinoma (11/45) followed by mucinous cystadenoma (9/45).

Conclusion: Neoplastic lesions were more common than non-neoplastic lesions, while benign tumours outnumbered the malignant ones. The commonest benign tumor was dermoid cyst and malignant was serous cystadenocarcinoma. The commonest non-neoplastic lesion was luteal cyst. Among histological types of ovarian tumors, surface epithelial tumors dominated the other types.
Poster Session I

THE DEVELOPMENT OF AN INNOVATIVE NURSE-LED OVARIAN CANCER SURVIVORSHIP CLINIC

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Background: Due to the increase in cancer incidence, patients living longer and the increased waiting times in clinic, it was necessary in 2011, to identify ways to deliver alternative follow up care for women with Gynaecological cancers. Patients were often travelling long distances and waiting for over four hours for what was quite often a routine follow up appointment with no further action.

Aim: To introduce an innovative Nurse-Led Service, that would re-define what Ovarian cancer follow-up should look like and deliver effective follow up care for women.

Method: In May 2011, following discussions, with the three Consultant Gynae-Oncologists, a nurse-led ovarian cancer survivorship clinic was established at Velindre Cancer Centre in Cardiff.

All women with ovarian cancer who had completed their chemotherapy were referred to the nurse-led clinic after discussion with their consultant. Clinic guidelines were developed and during the nurse-led clinic a full assessment is carried out following the eight domains of survivorship.

After a six month pilot of the clinic, it was audited through a patient satisfaction questionnaire.

Results: Thirty questionnaires were distributed to patients and twenty-five questionnaires were returned, giving a response rate of 83.3%, which showed 100% of patient satisfaction with the service provided.

Comments have included “Faultless”; “They were great , very respectful” and “How privileged and fortunate we are to have such a service in a uncertain time”.

Conclusions: To continue the survivorship clinic and expand to include other patients with Gynaecological malignancies.
Poster Session I

STEREOTACTIC BODY RADIOTHERAPY (SBRT) VS VOLUMETRIC MODULATED RAPIDARC™ RADIOTHERAPY (RA-IMRT) IN LYMPH-NODES RECURRENTE OF GYNAECOLOGICAL MALIGNANCIES

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Purpose: evaluation and comparison of RA-IMRT vs SBRT in the salvage treatment of isolated lymph node recurrences in patients affected by gynaecological cancer. Preliminary results in terms of local control rate (LC) and overall survival rate (OS).

Materials and methods: From January 2010 to September 2011, 15 patients affected by isolated lymph nodes recurrence of gynaecological cancer underwent salvage radiotherapy after conventional imaging staging with CT and 18-FDG-PET/CT. Two different radiotherapy techniques were used in this study: RA-IMRT (Rapidarc™ implemented radiotherapy Varian Medical System, Palo Alto, CA, USA) or SBRT (BrainLAB, Feldkirchen, Germany).

Sixteen nodes were treated: 6 with RA-IMRT and 10 with SBRT.

Five patients underwent CT scan and all patients underwent 18FDG-PET/CT for pre-treatment evaluation and staging.

The mean total dose delivered was 54.3 Gy (range 50-60 Gy with conventional fractionation and 27.4 Gy (range 12-40 Gy hypofractionation) for RA-IMRT and SBRT respectively.

Results: The patients were controlled with CT or 18FDG-PET/CT during the follow-up. After a mean follow-up of 5 months the local control rate was 92.8% (100% and 88.9% for RA-IMRT and SBRT respectively).

At the time of the analysis the overall survival was 92.3 % (80% for RA-IMRT and 100% for SBRT).

Conclusions: Our preliminary results showed that, the use of RA-IMRT and SBRT are an excellent local therapy for isolated lymph nodes recurrences of gynaecological cancer with a good toxicity profile and local control rate, even if any long term survivors would be expected. New treatment modalities like Cyberknife are also being implemented.
Poster Session I

IMMUNE MECHANISM OF DOSE-DENSE CHEMOTHERAPY FOR OVARIAN CANCER

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Purpose: Assess if dose dense (DD) chemotherapy with low dose cisplatin and paclitaxel has immune-mediated superior efficacy in comparison to maximum tolerated dose (MTD) regimen in the treatment of platinum-resistant ovarian cancer.

Patients and methods: Preclinical mouse tumor models were used to compare the therapeutic effect and toxicity of DD and MTD regimen. The generation of anti-tumor immune response by DD regimen was followed by identification of immune cell subset responsible for antitumor effect. The preclinical results demonstrated DD regimen had greater therapeutic effect than MTD regimen and therefore justified further investigation in patients. 14 patients with platinum-resistant relapse of ovarian cancer received DD chemotherapy consisting of weekly carboplatin (AUC2) and paclitaxel (60-80 mg/m$^2$) as the third or fourth-line treatment. Serum was collected over the course of treatment and serial IFN-$\gamma$ and IL-2 levels were used to determine CD8$^+$ T cell activation.

Results: Preclinical results indicate DD regimen is less toxic to the immune system, reduces immunosuppression by the tumor microenvironment, induces tumor recruitment of macrophages, and promotes tumor-specific CD8$^+$ T cell response, as determined by IL-2 and IFN-$\gamma$ secretion. Of the 4 patients with clinical response, 3 patients had higher serum levels of IL-2 and IFN-$\gamma$.

Conclusion: The therapeutic effect of DD chemotherapy relies on the preservation of the immune system and promotion of tumor-specific immunity, especially antitumor CD8$^+$ T cell response. The results of the present study suggest a novel mechanism of DD regimen, which might be a preferable option for platinum-resistant disease.
Poster Session I

EXPRESSION OF PDCD5 PROTEIN IN EPITHELIAL OVARIAN CANCER AND RELATED WITH SURVIVAL

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Aims: To explore the expression level of PDCD5 (Programmed Cell Death 5) protein in epithelial ovarian cancer tissues and to clarify the relationship between PDCD5 expression and clinicopathological date or patient survival.

Methods: The expression of PDCD5 protein was analysed by immunohistochemistry in 107 cases of epithelial ovarian cancer, 16 cases of benign ovarian neoplasma, and 11 cases of normal ovarian tissues. The image analysis system was used to measure the average optical desity. Clinical data were employed to carry on the patient survival analysis.

Results:

1. PDCD5 protein expression was higher in normal ovarian tissues and benign ovarian neoplasma, but lower in epithelial ovarian cancer tissues. Image analysis demonstrated that the expression of PDCD5 protein among the three groups had significant statistical differences (P < 0.05).

2. The expression of PDCD5 protein in different FIGO staging and histological grading of epithelial ovarian cancer tissues had significant statistical differences (P < 0.05), and were downregulated with the increasing of FIGO staging and histological grading.

3. There was strongly positive correlation between the strong or weak expression of PDCD5 protein and patient survival (P < 0.05, R = 0.731).

Conclusions: The PDCD5 protein has a close relation with occurrence, development and clinical prognosis of epithelial ovarian cancer.
Poster Session I

ELEVATED CANCER IMMUNO-INTENSITIES OF STRESS-INDUCED PHOSPHOPROTEIN1 (STIP1) ARE ASSOCIATED WITH POOR OUTCOMES OF PATIENTS WITH OVARIAN CANCER

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Objective: Stress-induced phosphoprotein 1 (STIP1) was recently identified as a potential tumor marker for human ovarian cancer. To explore the role of STIP1 in clinical management of ovarian cancer, we analyzed STIP1 immuno-intensities in cancer tissues and clinicopathological data in patients with ovarian cancer.

Methods: A total of 330 ovarian cancer specimens that were obtained from primary surgeries in our hospital between 2000 and 2005 were analyzed with immunohistochemistry. STIP1 immuno-intensities, analyzed in histoscore, were correlated with clinical parameters of the patients. Biological functions of STIP1 were verified by treatment of ovarian cancer cells with recombinant human STIP1 and neutralization of STIP1 with anti-STIP1 antibodies.

Results: Multivariate analysis showed that high STIP1 histoscores, advanced stages, clear cell carcinoma, residual disease >= 2 cm were significant prognostic factors. High STIP1 histoscores (>= 184) were significantly associated with poorer prognosis: mean survival time of 109 months versus 74 months in the groups of low and high histoscores, respectively (P < 0.0001). Furthermore, histoscores of grade III were significantly higher than that of grade I-II tumors (P < 0.0001), indicating that STIP1 reflected tumor aggressiveness. Treatment of ovarian cancer cells with recombinant STIP1 promoted cell proliferation and migration, supporting the autocrine and paracrine functions of STIP1.

Conclusions: STIP1 immuno-intensities of human ovarian cancer tissues may be a useful predictor for overall survival of the patients with ovarian cancer.
Poster Session I

ETHNIC DIFFERENCES OF HISTOLOGIC DISTRIBUTIONS FOR EPITHELIAL OVARIAN CANCER

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Background: Clinical trials of ovarian cancer are mostly conducted in North America and Europe. Knowing the distributional differences of baseline characteristics between these and other areas can better apply the trial results to other countries.

Methods: Using a prospectively collected administrative healthcare database in a single institute in Taiwan, we identified 826 patients diagnosed with epithelial ovarian cancer between 2000 and 2012 (n = 826). Demographic and histologic characteristics were compared between this healthcare database to a recently published GOG 218 trial (n=1873).

Results: Comparisons of following characteristics are presented. Age (median 54 yrs, vs. 60 yrs in GOG 218), GOG performance status (91.2% , vs. 92.9% for £ 1 score), debulking status for stage III (73.7%, vs. 45.9% for £ 1cm residual tumor), histologic types (52.4%, vs. 84.5% for serous type; 14.8%, vs. 3.1% for endometroid type; 15.3%, vs. 2.9% for clear cell type; 9.3%, vs. 1.1% for mucinous type), tumor grading (11.2%, vs. 4.3% for grade 1; 63.5%, vs. 15.2% for grade 2; 25.3%, vs. 73.1% for grade 3).

Discussion: There are prominent distributional differences of age, debulking status, histologic type (especially endometroid and clear cell type), and tumor grading of epithelial ovarian cancer between Taiwan and GOG 218 trial. Bridging studies for ovarian cancer should be performed when extrapolating of the foreign clinical data into Taiwan.

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<th>Taiwan (%)</th>
<th>GOG 218 (%)</th>
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<tr>
<td>Serous</td>
<td>52.4%</td>
<td>84.5%</td>
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<tr>
<td>Endometroid</td>
<td>14.8%</td>
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<td>Clear cell</td>
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<td>Mucinous</td>
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Serous Endometroid Clear cell Mucinous

Taiwan 52.4% 14.8% 15.3% 9.3%

GOG218 84.5% 3.1% 2.9% 1.1%
Poster Session I

OVARIAN CANCER IN CHILDREN AND ADOLESCENCE: TREATMENTS AND REPRODUCTIVE OUTCOMES

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Background: Ovarian cancer in children and adolescence is rare. Treatment outcomes and reproductive functions are interested.

Aims: To review ovarian cancer in children and adolescence at Siriraj Hospital in 20-year period.

Methods: Study was conducted in ovarian cancer patients less than 21 years old who had been treated at Siriraj Hospital from January 1990 to December 2009. Medical records were reviewed and relevant data such as age, presenting symptoms, surgery type, tumor size, FIGO stage, cancer histology, adjuvant treatment, results, and reproductive outcomes were recorded.

Results: 48 cases met the criteria. Mean age of patients was 16.4. Abdominal distension was the major symptom. 72.9% received conservative surgery. 91.6% of cases were germ cell tumors and the remaining cases were sex cord-stromal tumor and epithelial tumor. 25/48 cases presented in stage I disease. The most common used chemotherapy regimen for germ cell tumors was BEP.

Most of patients had favorable outcomes; 46/48 cases had complete remission and retained their good health at the time of the review. It had only one recurrent case and one dead case. The survival could not be analyzed due to limitation of cases. 10 of contacted patients got married, 3 of them had successful full-term pregnancies.

Conclusions: Ovarian cancer in children and adolescence is a rare disease. The most common cancer is germ cell tumor and the standard treatment is conservative surgery follow by combination chemotherapy. Return of ovarian function and fertility outcome are the topics of interest.
POSTER SESSION I

SECONDARY CYTOREDUCTIVE SURGERY WITHOUT POSTOPERATIVE CHEMOTHERAPY FOR RECURRENT OVARIAN CANCER

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Objective: To date there is no consensus for optimal treatment strategies in recurrent ovarian cancer. Majority of women who undergo secondary cytoreductive surgery (SCR) are also offered postoperative chemotherapy. In our centre, chemotherapy is not offered routinely if optimal cytoreduction is achieved at SCR. This study aims to identify prognostic factors and estimate survival in women who undergo SCR without post-operative chemotherapy.

Methods: This is a retrospective review of 43 women with 'platinum-sensitive' recurrent ovarian cancer who had SCR between January 2006 and June 2011. Demographic, clinical, histopathological, follow-up and survival data were recorded. Prognostic factors associated with overall survival (OS) were examined by univariate and multivariate analyses.

Results: Median (IQR) follow-up after SCR was 21 months (12-49), 37 women (86%) received no postoperative chemotherapy. Median OS was 59 months (95% CI 49-69) from date of primary diagnosis and 23 months (95% CI 11-35) from date of SCR in these women. The median OS was 27 months (95% CI 16-37) for complete cytoreduction (70%), 9 months (95% CI 3-15) for optimal cytoreduction (22%) and 4 months (95% CI 0-15) for suboptimal cytoreduction (8%). Three women had ≥grade 3 complications and there were no postoperative deaths. High grade disease (HR=6.92, 95% CI 1.29-37.03), sub-optimal cytoreduction (HR=11.25, 95% CI 2.04-62.21) and carcinomatosis (HR=13.44, 95% CI 2.33-77.67) were independent predictors of OS.

Conclusion: With maximum surgical effort and careful case selection, SCR without postoperative chemotherapy in women with 'platinum-sensitive' recurrent ovarian cancer, could be considered as treatment option in some cases.
Poster Session I

ROLE OF INTRA-OPERATIVE FLUID OPTIMISATION USING OESOPHAGEAL DOPPLER IN ADVANCED OVARIAN CANCER; EARLY POSTOPERATIVE RECOVERY AND FITNESS FOR DISCHARGE

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Background and aims: To determine the effect of fluid optimisation using oesophageal Doppler monitoring (ODM) when compared to standard fluid management in women who undergo major gynaecological cancer surgery. To determine whether this intervention is associated with reduced postoperative morbidity.

Methods: From January 2009 to December 2010, women undergoing laparotomy for pelvic masses were allocated into either fluid optimisation using intra-operative ODM, or to have standard fluid replacement without using ODM. Cases were selected from two surgeons to control for variability in surgical practice. All perioperative and postoperative management details were collected prospectively. Univariate and multivariate analyses were performed to quantify the association between the use of ODM with early mobilisation, resumption of oral diet, opening of bowel and fitness for discharge.

Results: A total of 198 women were operated by the two pre-specified surgeons. 79 women had fluid optimisation with ODM whereas 119 women had standard anaesthetic care. In women with advanced ovarian cancer, use of ODM was associated with earlier mobilisation (adjusted OR=3.27, 95% CI 1.04-10.23, p=0.04), earlier resumption of oral diet (adjusted OR=3.38, 95% CI 1.14-10.02, p=0.03), earlier bowel opening (adjusted OR=3.52, 95% CI 1.02-8.92, p=0.05) and earlier fitness for discharge (adjusted OR=3.03, 95% CI 1.03-8.92, p=0.04). No significant difference in postoperative complications was noted.

Conclusion: Use of ODM for intra-operative fluid optimisation in women during surgery for advanced ovarian cancer is associated with improved postoperative recovery leading to early discharge. Studies with adequate power are needed to investigate the role of ODM in reducing postoperative complications.
Poster Session I

POSTOPERATIVE VENOUS THROMBOEMBOLISM (VTE) FOLLOWING MAJOR LAPAROTOMY PROCEDURES IN GYNAECOLOGICAL ONCOLOGY - A 3-YEAR PROSPECTIVE COHORT STUDY

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Background and aims: VTE is a serious preventable complication associated with gynaecologic oncology surgery. To minimise risk of VTE, the current recommendation is low molecular weight heparin, compression stockings and sequential compression devices perioperatively, as well as the use of inferior vena caval filters prior to surgery in women with recent VTE. This study aims to determine the incidence and prognostic factors of VTE in women with suspected and known gynaecological cancer when these measures are already in place.

Methods: This is a prospective cohort study in women undergoing major laparotomy procedures for suspected and known gynaecological cancer. Demographic, surgico-pathological and postoperative in-hospital data were obtained. Prognostic variables were assessed using univariate and multivariate logistic regression models.

Results: A total of 359 consecutive women from January 2008 to December 2011 were included in this study. 24 (7%) women were affected by VTE postoperatively, 6 (2%) had deep vein thrombosis, and 18 (5%) had pulmonary embolism. The median age (IQR) was 66 (56-73). Out of 9 (3%) in-hospital deaths, 2 (1%) were confirmed to be due to pulmonary embolism. In multivariate analysis, age>60 yrs (OR=9.89, 95% CI 1.12-87.18, p=0.04), FIGO stage 3&4 (OR=3.67, 95%CI 1.10-12.29, p=0.04) and bowel surgery (OR=6.42, 95% CI 2.03-20.33, p=0.002) were independent predictors of VTE. Grade≥3 postoperative complications (OR=6.09, 95% CI 1.49-24.89, p=0.01) were also independently associated with postoperative VTE.

Conclusion: Better prevention of postoperative VTE after major gynaecological oncology surgery is clearly needed. Procedure-specific prognostic risk scores may help in recommending more targeted preventative protocols.
Poster Session I

SURGICAL MANAGEMENT OF BORDERLINE OVARIAN TUMOURS: LONG TERM OUTCOMES AND ECONOMIC EVALUATION

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Background and aims: Most borderline ovarian tumours (BOT) are associated with good long term survival outcomes. We evaluated the long term outcomes of women treated for BOT, determined the risk factors for recurrence or progression to invasive carcinoma and critically evaluated hospital costs of conservative management vs. radical treatment.

Methods: This is a retrospective review of all borderline ovarian tumours diagnosed and treated at our centre or referred within three months of primary surgery, from January 2002 to December 2006. Surgical, histopathological, follow up and survival data were obtained. To determine the cost effectiveness of follow up strategies for women with BOT, we obtained details of the resources used during surgery, hospital stay, and outpatient visits.

Results: A total of 84 women with borderline ovarian tumours were evaluated. Mucinous histology was most common, 54 (64%) women, followed by serous, 25 (30%). Conservative surgery was performed in 18 (21%) women. Two out of seven women with serous BOT, who had conservative surgery (29%), had recurrence. Both women were free from disease after secondary surgical treatment until last follow-up. The cost of follow-up, including the cost of completion surgery in the conservatively treated group, was £19,024 per patient compared to the cost of follow-up of £9066 in the radical surgery group.

Conclusion: Conservative surgery remains a valid option in young women wanting fertility preservation, however, the need for long term follow up and further treatment in these women maybe associated with increased overall cost.
Poster Session I

PREFERENCE STUDY: CHOICE OF ORAL OR INTRAVENOUS TREOSULFAN AND CLINICAL OUTCOME IN ELDERLY PATIENTS WITH RECURRENT OVARIAN CANCER: FINAL ANALYSIS

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Background and aims: There is an increasing interest in the management of elderly patients in oncology. The alkylating agent treosulfan is effective as oral (p.o.) and intravenous (i.v.) formulation for recurrent ovarian carcinoma. Primary aim of this study was to explore the individual preference and compliance of elderly patients (≥ 65 years) for p.o. or i.v. treosulfan. Secondary aims were to evaluate the activities of daily life (ADL)-score, toxicity, response and survival. We present the final analysis of patient's characteristics, treatment choice, compliance, clinical outcome and toxicities.

Methods: 123 Patients with platinum sensitive and resistant ovarian cancer had free choice of treosulfan i.v. (7000 mg/m² d1, q28d) or p.o. (600 mg/m² d1-28, q56d) for maximal 12 cycles (i.v.) or 12 months (p.o.). Indecisive patients were randomized. Toxicity was evaluated according to the NCI-CTC version 2.0.

Results: 119 patients received therapy and were able for analysis (median 72 years, range 65-87). 99 patients chose i.v. and 17 p.o., 3 were randomized to i.v. Most common hematological toxicities (grade 3/4) were thrombopenia (12.6%), leukopenia (10.1%) and neutropenia (5.9%). Most frequent non-hematological toxicities (grade 3/4) were ascites (7.6%), subileus (6.7%) and abdominal pain (4.2%). Median time to progression/overall survival was 5.2/7.8 months (i.v.), and 5.6/10.4 months (p.o.), respectively. No differences in the ADL-score between i.v. and p.o. treosulfan were observed.

Conclusions: Elderly patients with recurrent ovarian cancer favoured the i.v.-treosulfan administration (85%). Treosulfan therapy was generally well tolerated. There were no significant differences in patient's characteristics, clinical outcome and ADL-scores in both groups.
**Poster Session I**

**BORDERLINE OVARIAN TUMORS: A RETROSPECTIVE ANALYSIS OF 218 PATIENTS**

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**Objectives:** This study retrospectively reviewed the clinical outcomes of patients underwent different surgical procedures with borderline ovarian tumors at Obstetrics and Gynecology Hospital of Fudan University.

**Methods:** The clinical files of patients with borderline ovarian tumors from September 2003 to December 2010 were analyzed retrospectively (n=218). Evaluations were performed regarding by age, histological types, chief complaints, menstruation history, serum CA125 level, tumor size, FIGO stages and surgical procedures. Patients were stratified into three groups:

- Group I, radical surgery;
- Group II, unilateral salpingo-oophorectomy;
- Group III, cystectomy.

The post-surgical ovarian function, pregnancy rate and recurrence rate were evaluated among these groups.

**Results:** A total of 218 patients were enrolled for this study. Most of patients after fertility-Sparing surgery were in regular menstruation. Less menstruation flow occurred in 8 patients (6 patients in group II and 2 patients in group III, P>0.05). The decreasing complaint of menopausal symptoms, such as dysphoric, sweatiness, tidal fever were observed from group I to group II to group III (35.59%, 16%, 4.45%, respectively, P< 0.05). A total of 35 patients in the fertility-sparing groups desired to conceive after treatment. 9 cases in group II(81.82%) and 19 cases in group III(79.17%) successfully pregnant (P>0.05). The recurrence rate was much higher in group III (10.34%) than in group I (3.39%) and group II(4%), though without statistical significance (P>0.05).

**Conclusions:** Unilateral salpingo-oophorectomy and cystectomy are both safe and could result in low discomfortable complaint and high future pregnant rate, suggesting fertility-sparing surgery should be considered for younger patients.
THE EXPRESSION AND CLINICAL SIGNIFICANCE OF NDUFS3 IN HUMAN SEROUS OVARIAN CANCER

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Objectives: The aim of this study was to evaluate the expression and the clinical significance of nicotinamide adenine dinucleotide dehydrogenase Fe-S protein 3 (NDUFS3) in human serous ovarian carcinomas.

Methods: Totally Paraffin-embedded sections of 30 cases of normal ovarian tissues, 30 cases of benign serous ovarian tumor tissues and 111 cases of serous ovarian carcinomas were evaluated for NDUFS3 protein expression by immunohistochemistry, and Western-blot and real time RT-PCR were performed further to confirm the expression of NDUFS3. The correlation of NDUFS3 protein expression with clinicopathologic parameters and the probability of overall survival and disease-free survival were analyzed.

Results: NDUFS3 expression was significantly decreased in serous ovarian cancer compared with benign serous ovarian adenomas or normal ovarian epithelium (P< 0.001 for both). In addition, reduced NDUFS3 staining was significantly correlated with FIGO stages (P< 0.001), age (p=0.024), residual disease after primary surgery (p=0.003) and the clinical response to chemotherapy (p=0.025). Other clinicopathologic parameters were not significantly related to staining intensity. Moreover, low NDUFS3 expression was associated with poor disease-free survival (DFS) (P =0.04), while NDUFS3 expression was not associated with the overall survival (OS) (P =0.197). In multivariate Cox regression analysis, NDUFS3 expression not appeared to be an independent prognostic factor for survival of SOC patients.

Conclusions: NDUFS3 may play a role in the etiology and development of serous ovarian cancer, while the level of NDUFS3 protein expression appears to have a limited usefulness in predict the prognostic of SOC patients.
Poster Session I

AN UPDATED ASSESSMENT OF GLOBAL OVARIAN CANCER TRENDS

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Background: Ovarian cancer, the second most common gynecological malignancy, is the leading cause of gynecologic cancer-related deaths in Europe and the United States (US). Incidence and mortality rates have reportedly remained stable or slightly declined.

Aim: To describe recent trends in ovarian cancer incidence and survival in the US, and global rates of ovarian cancer.

Methods: Data from the US Surveillance, Epidemiology, and End Results (SEER) Program were used to describe ovarian cancer incidence rates and 12-, 24-, and 60-month survival. Annual percent change (APC) was calculated using NCI's Joinpoint regression program. Data from GLOBOCAN 2008 were used to project country-specific incidence rates in 2010 and 2020.

Results: From 1988-2008, there were modest, statistically significant, declines in ovarian cancer incidence in the US for women of all ages (APC: -1.03%), among women < 65 years (APC: -1.09%), and among women ≥65 years (APC: -0.95%). There were also small increases in survival at 12 (APC: 0.19%), 24 (APC: 0.58%), and 60 months (APC: 0.72%). Incidence rates varied widely, with the lowest rates in China (~10/100,000 for ≥65 years) and highest rates in the United Kingdom (~50/100,000 for ≥65 years) in 2010. In general, incidence rates were highest in Northern and Western Europe, North America, and Australia.

Conclusions: Incidence and survival were fairly stable over time in the US, as the percent changes were small. Globally, there was wide variation in incidence of ovarian cancer, which is consistent with previously reported associations of higher incidence in northern latitudes and industrialized countries.
Poster Session I

COMORBID CONDITIONS IN ELDERLY WOMEN WITH AND WITHOUT OVARIAN CANCER

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Background: For patients with cancer, comorbidities may affect their cancer treatment course and overall survival. These comorbidities may be present at cancer diagnosis or diagnosed shortly thereafter.

Aim: To estimate the prevalence and incidence of comorbidities among women with ovarian cancer (OvCa).

Methods: Patients ≥66 years with incident OvCa were identified in the SEER-Medicare dataset (1998-2002), and followed through 2005. Cancer-free women (controls) were matched by age and county of residence. Prevalence at diagnosis (%) and incidence rates [per 1,000 person-years (PY)] 3- and 12-months after diagnosis were calculated for each comorbidity (e.g. cardiovascular, gastrointestinal, metabolic, or pulmonary diseases). Results were also stratified by age and stage at diagnosis.

Results: Of the 5,087 OvCa patients identified, 58% were ≥75 years, and 67% had stage III/IV disease at diagnosis. There were few differences in comorbidity prevalence between OvCa patients and controls. However, the 3-month incidences (per 1,000 PY) of all comorbidities assessed were higher in OvCa patients than controls, and often increased with increasing age and stage at diagnosis. For example, the 3-month incidence of congestive heart failure was almost 10-fold higher in OvCa patients (290.5) versus cancer-free women (29.8), and diabetes was 65.8 in OvCa versus 15.8 in controls.

Conclusions: Our findings suggest that OvCa patients were often diagnosed with comorbidities after cancer, and these rates could be high and often increased with advanced cancer stage. This may be due to increased visits and testing after cancer diagnosis. Understanding the frequency of these conditions may help inform treatment decisions.
Poster Session I

METHYLATION ANALYSIS OF TUMOR SUPPRESSOR GENES IN OVARIAN CANCER

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Objective: Epigenetic changes are considered to be a frequent event during tumor development. Hypermethylation of promoter CpG islands represents an alternative mechanism for inactivation of tumor suppressor genes, DNA repair genes, cell cycle regulators and transcription factors. The aim of this study was to investigate promoter methylation of specific genes in ovarian cancer by comparison with normal ovarian tissue.

Methods: To search for epigenetic events we used MS-MLPA (Methylation-specific Multiplex ligation-dependent probe amplification) to compare the methylation status of 69 tissue samples of ovarian cancer with 40 control samples.

Results: Using a 15% cut-off for methylation, we observed significantly higher methylation in genes MGMT, PAX5, CDH13, WT1, THBS1, GATA5 in the ovarian cancer group, while in the ESR1 gene we observed significantly higher methylation in the control group compared with the ovarian cancer group.

Conclusion: These findings could potentially be used in screening of ovarian cancer, and may have implications for future chemotherapy based on epigenetic changes.

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Poster Session I

GENE EXPRESSION PROFILING OF NEWLY ESTABLISHED OVARIAN CANCER CELL LINES: IDENTIFICATION OF A FUNCTIONAL ROLE FOR S100A14 IN OVARIAN CANCER


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Purpose: To identify genes and proteins those are highly differentially expressed in epithelial ovarian cancer (EOC) cell lines, and to use this knowledge for the development of novel therapeutic markers for ovarian cancer.

Materials and methods: We have established 6 new EOC cell lines and characterized these by Illumina microarray platforms and two-dimensional gel electrophoresis (2-DE) and MALDI-TOF/PMF protein profiling. To validate the results of the microarray, SYBR green real-time PCR and immunohistochemistry (IHC) was performed. Subsequently, lentivirus-mediated overexpression and short hairpin RNA (shRNA) approaches were used for analysis of the biological functions of S100A14.

Results: We identified 859 genes that were commonly up-regulated and 1116 genes that were down-regulated in the cancer cell lines (> 2-fold, P < 0.05). In 2-DE and MALDI-TOF/PMF, 31 up-regulated spots were observed that had at least two-fold differences between the 3 EOC cell lines and HOSE cells used as controls. In cDNA microarray analyses, S100A14 was 6.29-fold overexpressed in ovarian cancer samples compared with the HOSE cells. Real-time PCR and IHC revealed S100A14 overexpression in ovarian cancers (P = 0.037 and P = 0.032, respectively). Lentivirus-mediated overexpression of S100A14 in TOV112D and YDOV-151 cells resulted in increased proliferation of ovarian cancer cells due to acceleration of cell cycle progression in connection with the upregulation of cyclins A and B1.

Conclusions: These data show the aberrant expression of S100A14 in ovarian cancer and that S100A14 may play a significant role in ovarian carcinogenesis.
Poster Session I

THE DIAGNOSTIC VALUE OF F-18 FDG PET/CT FINDINGS IN NONEPITHELIAL OVARIAN CANCER

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Objectives: To evaluate the diagnostic value of F-18 2-fluoro-2-deoxyglucose(FDG) positron emission tomography combined with computed tomography (PET/CT) in nonepithelial ovarian cancer.

Patients and methods: A retrospective chart review of 33 patients who were diagnosed nonepithelial ovarian cancer including granulose cell tumor(GCT, n=10), dysgerminoma(DG, n=4), mixed germ cell tumor(MGCT, n=3), Sertoli-Leydig cell tumor(SLCT, n=2), immature teratoma(IT, n=9) and yolk sac tumor(YST, n=5) and had preoperative PET/CT for diagnosis from January 2005 to December 2011 at our institution was conducted. We compared ratio (SUV(standard uptake value)max/liverSUV) and SUVmax according to diagnosis. And correlation between SUVmax, ratio(SUVmax/liverSUV) and tumor size, CA 125 level and stage was evaluated respectively.

Results: The ratio (SUVmax/liverSUV) (9.13±6.10) and the SUVmax(14.19±8.59) in mixed germ cell tumor had significant differences(P value=0.003, 0.002) compared with other nonepithelial ovarian cancer (GCT(1.61±0.50, 2.90±1.13), DG(3.98±7.67, 7.86±5.16), SLCT(2.36±1.05, 4.65±1.77), IT(3.81±2.07, 7.77±4.20), YST(3.78±1.35, 7.22±1.50)). There was positive linear correlation between CA 125(205.33±242.38) and SUVmax(P value=0.003), ratio(P value=0.002). And there was no significant correlation between SUVmax, ratio and tumor size(247.36±235.79(cm²)) and stage(3.40±3.00) respectively.

Conclusions: F-18 FDG PET/CT might have a role in discriminating nonepithelial ovarian cancer especially mixed germ cell tumor. Further study with large number of patients is needed to assess the diagnostic value of F-18 FDG PET/CT in nonepithelial ovarian cancer.
Poster Session I

DYSGERMINOMA IN A CASE OF 46, XY PURE GONADAL DYSGENESIS (SWYER SYNDROME): A CASE REPORT

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Dysgerminoma is uncommon in the pediatric age group. This malignancy can be associated with pure gonadal dysgenesis, primary amenorrhea, bilateral streak gonads in a phenotypic female.

We report the case of a 12-year-old XY woman who developed a bilateral dysgerminoma from undifferentiated gonads. The patient presented with 2 days history of periumbilical pain and RLQ pain. She had gone an ultrasonography, which showed a solid heterogeneous abdominopelvic mass of 10 * 6 cm size. MRI and PET-CT scan of whole body confirmed multiple retroperitoneal lymphadenopathy and malignant tumor arising from the right ovary. Additional evaluation was normal for serum CA 125, but AFP 26.78 ng/ml, LDH 3647 IU/ml, HCG 4.3 mIU/ml, FSH 28.7 mIU/ml. Past medical history in this patient was negative, except for no mencarche, Tennar stage 1. She underwent the right salpingo-oophorectomy, peritoneal washing, the biopsies of left ovary and staging, paraaortic and pelvic lymphadenectomy. Laparotomy revealed a normal (infantile) uterus and tubes. Pathology confirmed ovarian dysgerminoma of bilateral and no metastases to retroperitoneal nodes and tumor classified as stage Ib. After surgery, a preoperative karyotyping was reported as 46, XY. So, the first adjuvant chemotherapy that consisted of EC was administrated and then performed laparoscopic salpingo-oophorectomy of the right. Pathology revealed gonadoblastoma in left ovary and no residual malignancy for dysgerminoma. She received total four cycles of carboplatin-etoposide chemotherapy. At present, She remains disease-free 8 months after the surgery.

Conclusion: In girl with suspected dysgerminomas and premenarche, preoperative karyotyping should be done to avoid multiple surgical procedures.
OVEREXPRESSION OF CD73 IN EPITHELIAL OVARIAN CARCINOMA IS ASSOCIATED WITH BETTER PROGNOSIS, LOWER STAGE AND BETTER DIFFERENTIATION

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Purpose: The purpose of the current study was to evaluate survival outcome according to the expression status of CD73 in patients with epithelial ovarian cancer.

Methods: A total of 167 patients with epithelial ovarian cancer were enrolled in the current study. For each patient, a retrospective review of medical records was conducted. Immunohistochemical staining for CD73, CD8, FoxP3, and CD68 was performed using tissue microarray made with paraffin embedded tissue block.

Results: 29.9% of (N = 50) patients showed negative expression for CD73, whereas 70.1% of patients (N = 117) showed positive expression for CD73. The CD73 positive group showed better prognosis compared to the CD73 negative group (5 year overall survival of CD73 positive group: 73.0% and that of CD73 negative group: 50.1%, p=0.023). CD73 was more frequently expressed in mucinous adenocarcinoma and clear cell carcinoma compared to serous or endometrioid adenocarcinoma. In addition, CD73 overexpressions were more frequently detected in patients with known good prognostic factors, i.e., low stage, well/moderate differentiation, negative peritoneal cytology, no lymphovascular involvement, and no macroscopic residual tumor after debulking surgery. There was significantly more infiltration of regulatory T cells in the CD73 negative group compared to the CD73 positive group.

Conclusion: Good prognosis in patients with overexpression of CD73 might be due to that overexpression of CD73 was more frequently observed in epithelial ovarian cancer patients with known good prognostic factors. Therefore, the result of our study means that favorable differentiation and stage have more influence on survival outcome than adverse effect of CD73 per se on the host's local immune system.
Poster Session I

ANALYSIS OF SECRETOME PROTEIN MODIFICATIONS IN OVARIAN CANCER CELLS

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Introduction: The secretome proteins that control and regulate physiological processes, exhibit as a clinically relevant source for therapeutic target in ovarian cancer. The expressed specific protein secreted from ovarian cancer cells can be recognized.

Objective and aims: We characterized the secretomes of OVCAR3 cells under serum-free culture conditions. We have been undertaking an approach to characterize post-translational modifications (PTM) as potential protein markers. In combination with amino acid sequence, post-translational modifications help to define the primary structures of proteins.

Methods: Cell extracts from VGH-OVCAR-3 cells cultured with serum versus serum-free were subjected to 2D electrophoresis. The different spots were extracted. Using tandem mass spectrometry (LC/MS/MS) to analyze the extracts, we have identified some post-translational modifications in secreted proteins from ovarian cancer cell line OVCAR-3.

Results: The secretomics constituents indeed are different from those from serum-deprived cells, indicating the potential application of this technique in cancer biology studies. Post translational glycosylation and hydroxylation of protein CPC, as well as phosphorylation at M1347 of ITIH2 protein were detected.

Conclusions: PTM identification of proteome could be recognized as putative screening markers of ovarian cancer.
Poster Session I

MALIGNANT OVARIAN GERM CELL TUMOURS DOWN UNDER: THE AUCKLAND EXPERIENCE 1997-2010

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Objective: Malignant ovarian germ cell tumours (MOGCT) are aggressive yet highly curable malignancies predominantly affecting young women. This study was performed to compare the outcomes of our institution with published international series.

Methods: A retrospective study of patients presented at our tertiary institution's Gynaecological Multidisciplinary Meeting between 1997 and 2010 was performed. Patients with MOGCT were identified and data on surgery, histology, stage, treatment, toxicity and survival was collected.

Results: 40 patients were identified. Median age at diagnosis 27 years (14-44 years). Histology: immature teratoma 47.5%, yolk sac tumour 27.5%, dysgerminoma 12.5%, mixed germ cell 7.5%, neuroectodermal 2.5% and embryonal 2.5%. 62.5% were stage I, 10% stage II, 20% stage III and 7.5% stage IV.

Initial surgery was performed outside a tertiary centre in 63%. Thirty two women (80%) underwent fertility sparing surgery.

75% of women had adjuvant chemotherapy; with 97% receiving Bleomycin, Etoposide and Cisplatin (BEP). 10 patients (25%) elected for intensive surveillance with none recurring. Median follow up was 56 months (4-164). Two patients with stage IV disease were primary platinum refractory and died at 4 and 9 months. No patients had recurrent disease. The overall survival was 95%.

Conclusions: Our modern series highlights the improving overall outcomes for women with MOGCT’s with respect to preserving potential fertility and reducing toxicities, whilst maintaining excellent prognosis. Fertility sparing surgery, appropriate chemotherapy or surveillance, minimization of toxicity and recognition of long term survivorship issues are crucial factors for optimal management of this highly curable but rare disease.
Poster Session I

THE VALIDATION OF MICRORNA PROFILING IN FROMALIN-FIXED, PARAFFIN-EMBEDDED OVARIAN CANCER SAMPLE

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Purpose: MicroRNAs are known as non-coding RNA molecules working for post-transcriptional regulation with critical biologic functions including differentiation, proliferation, apoptosis and stress resistance of cell. Owing to the unique riboregulatory function of gene expression, global microRNA profiling of human malignancies, especially extracted from formalin-fixed, paraffin-embedded (FFPE) samples, are increasingly carrying out. To assess the validation of FFPE ovarian cancer tissues for microRNA profiling, we compared the expressions of microRNAs of FFPE samples of ovarian cancer to those of matched fresh-frozen samples.

Method: Three patients operated for benign uterine disease (control group) and five patients diagnosed with serous ovarian carcinoma between June 2009 and October 2011 were enrolled. Profiling of microRNAs of each patient’s FFPE samples and matched fresh-frozen samples were performed using DNA microarray. Then the expression of eight over-regulated microRNAs and six down-regulated microRNAs were quantitatively analyzed by real-time PCR.

Result: We demonstrated using DNA microarray that the pattern of microRNA expression profiles of FFPE samples in ovarian cancer are comparable to those of fresh-frozen samples, with a significant correlation of up to 0.97. (p< 0.001) Among eight over-regulated microRNAs, six microRNAs were demonstrated more than control group as a same pattern in both FFPE and matched fresh-frozen sample. All the six down-regulated microRNAs were less demonstrated as a same pattern in both samples.

Conclusion: The profiling of microRNA in fromalin-fixed, paraffin-embedded ovarian cancer sample is valid as fresh-frozen sample.
**Poster Session I**

**HIPEC FOR OVARIAN CANCER RELAPSE: A FRENCH MULTI CENTER RANDOMIZED TRIAL ONGOING**

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**Background:** Most patients with advanced ovarian cancer experience a relapse. Standard treatment with chemotherapy provides a median 29 months overall survival (OS). Several clinical series suggested a benefit of secondary complete surgery (SCS). Prospective series with SCS and HIPEC have shown long survival, may be due to selection bias. HIPEC is a heavy treatment that needs to prove efficiency in a large randomized trial. CHIPOR (Chemotherapy and HIPEC for Ovarian cancer Relapse) is aimed to assess OS for ovarian cancer first relapse treatment.

**Patients and methods:** CHIPOR is a prospective multi center randomized phase III trial comparing 6 cycles of second-line platinum based chemotherapy, and SCS with or without HIPEC (Cisplatinum, 75mg/m², 42°C during 1 h). Randomization is performed during SCS only for patients with complete surgery. In order to show a one year benefit in OS we need to include 220 patients in each group (with or without HIPEC). Inclusion criteria are first ovarian cancer relapse, ≥6 months after initial treatment, without extra abdominal localization, platinum based second-line chemotherapy. A pharmacokinetic study will evaluate both absorption of cisplatin from peritoneal cavity to systemic compartment and cisplatin plasma exposure.

**Results:** 15 French Center are open since September 2011, and recently 1 center in Spain, and 1 in Belgium. At the end of March 2012, 25 patients were included.

**Conclusion:** CHIPOR is the first randomized trial aimed to assess the role of HIPEC for ovarian cancer relapse.
Poster Session I

BORDERLINE EPITHELIAL TUMORS OF THE OVARY: EXPERIENCE OF 55 PATIENTS


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Objective: The objective of this study was to evaluate the clinicopathologic features and the survival estimates in patients treated for borderline ovarian tumor (BOT).

Methods: We performed a retrospective review of all patients treated for BOT at our Institution from 1991 to 2011. Data were obtained from hospital records and gynecologic oncology charts.

Results: A total of 55 patients were identified. The median age was 40 years (range 13-79). The majority of patients (85.4%) had FIGO stage I disease and the remainder of them had FIGO stage II/III (7.3% in both stages). Serous histology was found in 58.2% of cases and abnormalities of CA 125 serum level occurred in 23.6% of them. All women underwent surgery and 3.7% of them received chemotherapy. 11% had a recurrence and the median survival rate was 39 months. The median survival and the 5 year survival rate of the all population was 42 months (range 16-84) and 97%.

Conclusion: BOTs have an excellent prognosis. Conservative surgery should be considered for women in the reproductive age group who desire preservation of fertility. A long-term follow-up is highly recommended for these tumors.
Poster Session I

DIFFERENTIALLY EXPRESSION OF MIRNAS AND TARGETS IN PATIENTS OF OPSC FROM OCC

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Objectives: To identify the key miRNAs and targets in patients of ovarian papillary serous carcinoma (OPSC) and ovarian clear cell carcinoma (OCC), for the insight of possible regulation gene and pathway of epithelial ovarian cancer (EOC) prognosis.

Methods: The study was opened to patients with primary, previously untreated EOC referred to member institutions. High-throughput analysis of the miRNA profile in a panel of OCC and OPSC cells was assessed using a microarray platform. The key miRNAs were further confirmed by quantitative Real-Time Polymerase Chain Reaction (qRT-PCR). The targets and possible pathway were predicted by TargetScans, MicroCosm Targets version 5, miRBase and Ingenuity. The top target, activating transcription factor 3 (ATF3) was validated by qRT-PCR and immunohistochemical (IHC) assay.

Results: Of 667 miRNAs analyzed, 83 were identified as enriched in the OPSC, and 15 in OCC (P< 0.01 for all). Seventeen of 667 miRNAs were significantly expressed with at least 3 fold differences in the OPSC versus OCC. The expression of tree miRNAs (miR-30a*, miR-30e*, miR-505*) were most significantly lower in OCC comparing to OPSC patients. ATF3, the top target of the key miRNAs mentioned above was highly expressed in OCC lesions, and a stronger distribution was shown in protein level of ATF3 by immunohistochemistry in OCC than OPSC lesions.

Conclusions: We identified the key miRNAs that differentially expressed in patients of OPSC and OCC tumors, validated the most popular target shared by the key miRNAs, indicating the possible regulation gene and pathway for EOC prognosis.
SURVIVAL ANALYSIS OF PATIENTS IN STAGE III OVARIAN CANCER

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Objective: Analyze survival of different categories of stage III ovarian cancer. The therapeutic value of lymphadenectomy has also been evaluated.

Material and methods: 140 patients with stage III-IV ovarian cancer in the last 30 years. Mean age was 54 years. 26,4% of the patients were asymptomatic. The more frequent symptoms were abdominal pain (29,3%) and abdominal swelling (21,4%). Surgical treatment was performed in 86,5%, being 10,7% only diagnostic, 7,9% suboptimal surgery (SOpS), and 67,9% optimal surgery (OpS). In survival analysis were considered stages IIa, IIIb and stage IIIc as negative lymph nodes (NLN), positive lymph nodes (PLN) and lymph node status unknown (ULN). Survival were compared with stage IV and between themselves. Results were adjusted by age and type of surgery.

Results: Overall 5-year survival for stage III was of 53,6%. The 5-year survival for stage Ila, IIb, IIIc(NLN), IIIc(PLN) and IIIc(ULN) were respectively of 82,4%, 57,1%, 92,9%, 66,7% y 30,3%. In stage IV was of 23%. Survival for stage IIIc(NLN) was better than the rest of the stage IIIC and stage IV. Survival for patients stage IIIc(ULN) was the same than stage IV. According the surgical approach, for patients with OpS survival was 58,3% compared with only 9,1% for patients with SopS.

Conclusions: Survival in stage IIIc(ULN) is similar to those in stage IV and significant lower than the rest of stage IIIC. Lymphadenectomy in cytoreductive surgery for ovarian cancer can has a therapeutical benefit since the lack of lymph node study has an influence in survival.
Poster Session I

CA 19-9 IS A NON VALUABLE MARKER THAT CAN INCREASE FALSE POSITIVE IN EVALUATION OF OVARIAN NEOPLASM

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Introduction: The tumor marker Ca-125 is widely used for diagnosis and prognostication of ovarian malignancies. Many clinicians routinely assess Ca19-9 levels to predict whether a primary ovarian tumor is benign, borderline or malignant, but limited studies have proven its clinical advantage.

Objective: To assess the clinical value of Ca19-9 in the triage of patients with ovarian neoplasm.

Methods: 393 patients with ovarian neoplasm were identified in which a preoperative serum Ca19-9 and Ca-125 level had been measured. All these patients underwent surgery. A correlation between tumor marker levels and final histology was performed.

Results: Seventy-three of 393 patients (18.6%) had elevated CA 19-9. According to the histology findings, Ca 19-9 levels were increased in 11.5% of benign cases, 22.3% of malignant neoplasms, 27.7% of borderline tumors and 40% of metastatic tumors. There was no correlation between the serum Ca19-9 levels and the histology results. The sensitivity of Ca-125 in predicting malignancy was 84.9%, with a false positive of 21.5%. The addition of cases with elevated Ca19-9 and normal Ca-125 increased the sensitivity by 2.9 %, with a false positive of 57%.

Conclusions: Our data suggest that Ca 19-9 is not a valuable marker to predict whether a suspected ovarian neoplasia is benign or malignant. Due to the elevated false positive we do not recommend using this marker in evaluation of ovarian neoplasm.
EXTRA-OSSEOUS EWING'S SARCOMA PRESENTING AS INTRA-ABDOMINAL TUMOR IN YOUNG WOMAN

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Ewing's sarcoma/primitive neuroectodermal tumor (ES/PNET) is part of a rare group of malignant neoplasms with small round-cell morphology. Extra-skeletal or extra-osseous ES/PNET is morphologically indistinguishable from Ewing sarcoma of bone. We report a rare case of extraskeletal Ewing's sarcoma diagnosed in a 25-year-old woman presenting with an abdominal distension. She had a large intra-abdominal tumor on ultrasound and MRI, thought to be ovarian tumor. She underwent surgical exploration, which confirmed a malignancy, but the exact etiology was uncertain. Final pathology was consistent with extra-skeletal ES/PNET. Histopathology revealed an anaplastic small-round-cell tumor with diffuse membranous CD99 immunoexpression. ES/PNET of the abdominal cavity is an unusual diagnosis. A review of the literature indicates that extra osseous ES/PNET requires early diagnosis and multimodality treatment including surgery, chemotherapy, and radiotherapy. After surgery, the patient was treated with four cycles of chemotherapy based on vincristine, doxorubicine, cyclophosphamide, MESNA and was scheduled for radiotherapy. Despite its rarity, the differential diagnosis of intra-abdominal mass must be considered in young women.
Poster Session I

FOLLICULAR VARIANT OF PAPILLARY THYROID CARCINOMA ARISING FROM DERMOID CYST

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Objective: Benign or mature cystic teratomas, also known as dermoid cysts, are composed of mature tissues, which can contain elements of all three germ cell layers. Malignant transformation of mature cystic teratoma is more common in postmenopausal women however can also be rarely identified in younger women. We present a rare case of a 19-year-old woman with malignant transformation of an ovarian mature cystic teratoma.

Case report: Our case was a 19-year-old woman, who was diagnosed postoperatively with follicular variant of papillary thyroid carcinoma in mature cystic teratoma. She underwent right cystectomy for adnexal mass. Postoperative metastatic workup revealed a non-metastatic disease and the patient did not undergo any further treatment. After two months operation, near-total thyroidectomy performed in our case. The patient is currently followed with serum thyroglobulin and is asymptomatic.

Conclusion: Malignant transformation of dermoid cyst is a rare ovarian neoplasm. We believe that unilateral oophorectomy or cystectomy is a reasonable treatment option for cases in which there is no evidence of capsular invasion, vascular invasion or gross metastasis, and preservation of fertility is desired. Total thyroidectomy was diagnosed in selected cases. Serial serum thyroglobulin should be used as a tumor marker for follow-up.
Poster Session I

RETROSPECTIVE COMPARISON OF 10 MORPHOLOGICAL SCORING SYSTEMS IN OVARIAN MALIGNANCY: AN EXTERNAL VALIDATION OF GRAYSCALE SONOGRAPHIC PREDICTION MODELS

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Aim: The purpose of this study was to evaluate the ability of six morphological scoring systems and four morphological classification systems to detect malignant ovarian tumors.

Materials and methods: This is a retrospective study of 320 women admitted to the Department of Obstetrics and Gynecology of Gülhane Military Medicine Academy for surgical exploration of pelvic masses. To diagnose malignant ovarian tumors, the sensitivity, specificity, negative and positive predictive values and diagnostic accuracy of six morphological scoring systems (Sassone et al., DePriest et al., Lerner et al., Ferrazzi et al., Ueland et al., Szpurek et al.) and four morphological classification systems (Finkler et al., Granberg et al., Maggino et al., Valentin et al.) were obtained.

Results: Out of 320 operated patients, 80 were malignant. When we insisted on perfect sensitivity, the highest specificity were 0.65. In our study we observed that the performance of the existing models to be inferior to the performance reported in the initial studies.

Conclusion: We concluded that any of the ten systems described can be used for selection of cases for optimal therapy. These methods are simple techniques that can be used even in less-specialized gynecology clinics to facilitate the selection of cases for referral to an oncological unit.
Poster Session I

OVARIAN CARCINOMA PRESENTING WITH ISOLATED INGUINAL LymphNODE METASTASIS IN NORMAL SIZE OVARIES: A CASE REPORT

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Introduction: It is generally recognized that ovarian cancer tends to remain intraabdominal even in advanced stage. We came across a woman with ovarian carcinoma who presented with a fungating left groin swelling.

Case history: A 35yrs para2 women presented with a fungating left inguinal node of 5X4 cm for last 3 months. Biopsy revealed metastatic papillary adenocarcinoma. Clinical examination showed left sided pedal oedema. Laboratory investigation reveled increased CA125(412IU/ml). Radiological studies were normal.

Treatment and outcome: In view of the raised Ca 125 she was treated in the lines of FIGO stage III cancer ovary with Paclitaxel 200mg and Carboplatin 300mg for three cycles. She responded dramatically with completely healed inguinal nodes. Then laparotomy with total hysterectomy, bilateral salpingo-oophorectomy and partial omentectomy were performed. Histology confirmed left ovarian adenocarcinoma consistent with the earlier histology of the left inguinal lymph node. There were no other sites of involvement. Postoperatively, the patient received three more cycle of chemotherapy.

Conclusions: Ovarian cancer presenting with inguinal lymph node metastases is uncommon. About 1% ovarian carcinoma may have a normal sized ovary. Further, ovarian cancer manifesting as isolated inguinal lymph node metastasis with a normal size ovary is extremely rare. This case demonstrates that early distal metastasis, although rare, can occur in patients with ovarian cancer and may be a presenting symptom.
Poster Session I

FOLATE RECEPTOR ALPHA: POTENTIAL THERAPEUTIC TARGET FOR PURE YOLK SAC TUMORS AND MIXED GERM CELL TUMORS WITH YOLK SAC COMPONENT

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Objective: Folate receptor alpha (FRA) has restricted expression in normal cells but is highly expressed in various non-mucinous tumors of epithelial origin, including epithelial ovarian carcinoma. The lack of data on FRA expression in rare ovarian histotypes, prompted us to evaluate FRA expression in non-epithelial ovarian cancer.

Materials and methods: Expression of FRA was analyzed using Mab 26B3 in 18 non-epithelial ovarian cancers, including 11 sex-cord stromal tumors (8 granulosa cell, 2 sertoli cell and 1 leydig cell tumor) and 7 germ cell tumors (2 yolk sac tumors, 2 mature teratomas, 1 dysgerminoma and 2 mixed germ cell tumors with yolk sac component). The FRA expression was analyzed using a weighted intensity score for immunohistochemical tumor cell membrane staining (range 0 for no to a maximum of 50 for 100% membrane staining).

Results: FRA expression was completely negative in sex-cord stromal tumors. Among the germ cell tumors, pure yolk sac tumors and mixed tumors with a yolk sac component showed a higher FRA expression (median M-score 12.5, range 6.7-28.3) than those without yolk sac component (median M-score 0.0, range 0.0-1.2).

Conclusions: Although the numbers are small, FRA expression in non-epithelial ovarian cancer seems to be limited to pure yolk sac tumors and mixed germ cell tumors with a predominant yolk sac component. The FRA might therefore become a potential target for diagnostic and therapeutic purposes in those tumors.
Poster Session I

FOLATE RECEPTOR ALPHA EXPRESSION REMAINS UNCHANGED IN EPITHELIAL OVARIAN CANCER: COMPARISON OF BIOSPIES AT DIAGNOSIS AND AFTER CHEMOTHERAPY

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Objective: Based on its increased expression, folate receptor alpha (FRA) is an attractive candidate for targeted diagnostics and therapeutics in non-mucinous epithelial ovarian cancer (EOC). However, applicability of these agents in residual or recurrent disease could be influenced by the effect of chemotherapy. We evaluated whether chemotherapy modified FRA expression in non-mucinous EOC.

Materials and methods: 81 EOCs, of which 71 serous, 10 non-serous (4 clear cell, 3 endometrioid and 3 mixed), and 10 benign cases (5 normal ovarian tissues, 5 benign cysts) were assessed for FRA immunohistochemical staining using MAb 26B3 and a weighted intensity score (M-score, range 0-50) was calculated. Chemotherapy effect was evaluated in 24 patients with tissues from both primary and interval debulking surgery, and 10 patients with samples from both primary and recurrent disease.

Results: Primary EOC showed higher FRA expression than non-neoplastic ovaries (median M-score 41.7 vs 0.0). FRA was highly expressed in 78% of ovarian cancers at diagnosis and 87.5% after chemotherapy exposure. Paired samples from both primary and interval debulking surgery did not differ in FRA expression (median M-score 41.7 vs 40.0). Recurrent tumors also reflected the FRA status at diagnosis (median M-score 45 vs 41.7).

Conclusions: This study shows no significant difference in FRA expression after chemotherapy exposure, strengthening the rationale for FRA targeted diagnostics and therapeutics in the treatment of EOC patients, whether newly diagnosed or at recurrence. Furthermore the data suggest that immunohistochemical FRA analysis at diagnosis can guide the decision whether to use FRA targeted therapy upon recurrence.
Poster Session I

SYSTEMATIC PARA-AORTIC AND PELVIC LYMPHADENECTOMY IN EARLY STAGE EPITHELIAL OVARIAN CANCER: A PROSPECTIVE STUDY

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Background: Lymphadenectomy is important in the surgical treatment of apparent early epithelial ovarian cancers (eEOC); however its extent is not well defined. We evaluated the role of systematic lymphadenectomy, the risk factors related with lymph node metastases, the implications and morbidities of comprehensive surgical staging.

Methods: We prospectively recruited 124 patients diagnosed with apparent eEOC (FIGO stage I and II) between January 2003 and January 2011. Demographics, surgical procedures, morbidities, pathologic findings and correlations with lymph-nodes metastases were assessed.

Results: A total of 111 patients had a complete surgical staging including lymphadenectomy and were therefore analyzed. A median of 23 pelvic and 20 para-aortic nodes were removed. Node metastases were found in 15 (13.5\%) patients. Para-aortic region was involved in 13/15 (86.6\%) of cases. At univariate analysis age, menopause, FIGO stage, grading and laterality resulted as significant factors for lymph-node metastases, whilst CA 125 > 35 U/ml and positive cytology did not. No lymph node metastases were found in mucinous histotype. At multivariate analysis only bilaterality (p: 0.018) and menopause (p: 0.032) maintained a statistically significant association with lymph node metastases. Lymphadenectomy related complications (lymphocysts formation and lymphorrea) were found in 14.4\% of patients.

Conclusions: The data of this prospective study demonstrate the prognostic value of lymphadenectomy in eEOC. Menopause, age, bilaterality, histology, and grading of the tumor are identifiable factors that can help, in the decision whether or not to do comprehensive surgical staging with lymph node dissection. These parameters may be used as surrogates for treatment planning.
Poster Session I

BORDERLINE CLEAR CELL TUMOR OF PERITONEAL ENDOMETRIOSIS

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Introduction: Endometriosis which affects up to 10% of reproductive age women is known to increase the risk of ovarian cancer. Most commonly detected endometriosis-associated ovarian cancers (EAOCs) are clear cell and endometrioid type adenocarcinomas. In case of malignant transformation of an extraovarian endometriosis, endometrioid type is the most commonly encountered histology.

Objective: To emphasize the significance of endometriosis and its malign transformation, a case with borderline clear cell tumor within an endometriotic focus is presented.

Case report: A 36-year-old nulliparous woman with a history of two previous surgeries for endometriosis admitted with chronic pelvic pain and infertility. Transvaginal ultrasonography revealed a pelvic mass measuring 7 cm. CA 125 and CA 19-9 levels were elevated (251 U/ml and 47 U/ml, respectively). Laparotomy was performed. A pseudocyst measuring 7 cm on the left side of the pelvis and a solid mass measuring 4 cm on anterior pelvic peritoneum were detected and completely excised. Uterus and bilateral ovaries were normal and spared. Pathologic examination revealed peritoneal borderline clear cell tumor associated with endometriosis.

Conclusion: Endometriosis associated malignancies are mostly of ovarian origin, but a quarter of these malignancies involve extraovarian tissues, rectovaginal septum being the most common site. Hormonal therapy and atypical endometriosis are risk factors for malign transformation. Although EAOC is commonly diagnosed at early stages and has better survival, data regarding extraovarian malignant transformation is very limited due to its rarity. Primary approach should be wide excision followed by adjuvant therapy. To best of our knowledge there is no report of borderline clear cell neoplasia of peritoneal (extraovarian) endometriosis. Despite of the potential risk of malignant transformation, fertility sparing surgery could be performed in such cases if fertility is desired.
Poster Session I

COMPARISON OF OPTIMAL CYTOREDUCTION RATES WITH STANDARD AND MORE EXTENSIVE SURGERY IN ADVANCED OVARIAN CANCER

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Introduction: Ovarian cancer is the leading cause of death among women with gynaecological malignancies. Standard surgery achieves suboptimal cytoreduction (that is macroscopic residual disease) in over 80% of cases. The role of extensive cytoreductive surgery versus standard surgery in ovarian cancer treatment is still open to debate.

Objectives: Our aim was to evaluate the effectiveness of extensive surgery in achieving optimal cytoreduction (less than 1 cm residual disease) in advanced stage ovarian cancer.

Design: Retrospective review and analysis.

Setting: New diagnoses of ovarian cancer referred to University College London Hospital (UCLH) during the period January 2006 to December 2010.

Methods: We analysed retrospective data on women with stage 3c or 4 advanced epithelial ovarian cancer who underwent either extensive or standard surgery.

Results: We identified 245 patients with stage 3c (n= 164) or 4 (n= 81) disease. 75 patients had primary laparotomy and 88 patients had interval debulking surgery (IDS). Of these 49 patients (30%) had extensive surgery, achieving optimal cytoreduction in 86% of cases. 109 patients (67%) had standard surgery, achieving optimal cytoreduction in 69% of cases.

Conclusions: The prognostic value of optimal surgical debulking is well reported and has been confirmed in a meta-analysis. Most of our patients continue to undergo standard surgery. However, extensive surgery in advanced ovarian cancer achieves higher rates of optimal cytoreduction when compared to standard surgery.
Poster Session I

ASSESSMENT OF TREATMENT IN PATIENTS WITH RECURRENT OVARIAN CANCER USING PET-CT: POTENTIAL CHANGE OF DISEASE FREE INTERVAL AND CHEMOTHERAPEUTIC REGIMEN

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Background: Therapeutic strategies are made a selection in view of disease-free interval (DFI) for patients with recurrent ovarian cancer. This principle is based on the results of clinical trials 20 years ago. The main imaging modality was CT-scan in these days. However, it is possible to detect recurrent lesion promptly by introduction of PET-CT. Therefore, DFI might shorten, and choice of chemotherapeutic regimen might alter.

Objective: To investigate whether PET-CT shortened DFI in patients with recurrent ovarian cancer.

Patients and methods: Between September 2009 and March 2011, thirty ovarian cancer patients who underwent PET-CT included in this study. Data were collected from the electric medical records included sequential serum CA 125 level, surgical debulking status, platinum sensitivity status, chemotherapeutic regimens, and efficacy of treatment.

Results: Thirteen patients got a diagnosis of recurrence. Eighty-five percent (11/13) had PET-CT on the ground that CA 125 became elevated. PET-CT findings were peritoneal dissemination (n=8), retroperitoneal lymph node metastasis (n=6), inguinal node metastasis (n=1), and lung metastasis (n=1). Median DFI was 10.7 month (range 7.5 - 21.6 mo). Response rate in case with DFI more than 12 months (100%) were better than those with DFI less than 12 months (57%). There were no recurrence cases with DFI less than 6 months. The other 17 patients had persistent disease.

Conclusion: There was no alteration of chemotherapeutic regimen in this case series. Further investigation is needed.
Poster Session I

PROSPECTIVE STUDY USING THE RISK OF OVARIAN MALIGNANCY ALGORITHM FOR DETECTION OF OVARIAN CANCER IN EGYPT

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Background: Ovarian cancer accounts for about 4% of all cancers among women. Due to its vague symptoms, ovarian cancer is usually diagnosed at advanced stages.

Cancer antigen 125 together with ultrasound have been proposed for early diagnoses. However low sensitivity and specificity are drawbacks to this approach. Human epididymis protein 4 has been proposed as a tumor marker for ovarian cancer. Results of previous studies have suggested that HE4 has diagnostic sensitivity similar to CA 125, but an increased diagnostic specificity in patients with gynecological malignancies. Combination of both markers using the Risk of Ovarian Malignancy algorithm increases the sensitivity and specificity of ovarian malignancy.

Aim: To evaluate the sensitivity, specificity and predictive values of the risk of ovarian malignancy algorithm (ROMA) in detection of ovarian cancer in patients with suspicious pelvic mass.

Methods: The study included 100 women presented by adnexal mass and treated surgically. These patients subdivided into two groups; first group included 50 patients with suspicious adnexal masses. Second group also included 50 women with non-suspicious adnexal masses. Each was subdivided into 2 groups according to parameters assessed.

Results: The sensitivity of CA125, HE4 and ROMA were 78.5, 81 and 82.5% while e specificity of CA125, HE4 and ROMA were 69.5, 74 and 75%. PPV of CA125, HE4 and ROMA were 75, 80 and 82%. NPV were 70, 75.5 and 76.2%.

Conclusions: Data indicates that ROMA might be of high importance in diagnosing ovarian cancer at early stages of the disease.
Poster Session I

COMPARISON OF OPTIMAL CYTOREDUCTION RATES IN EMERGENCY VERSUS NON-EMERGENCY ADMISSIONS FOR ADVANCED OVARIAN CANCER: A MULTI-INSTITUTIONAL STUDY

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Purpose:

i) To investigate whether first referral to the Emergency Department (ED) of a General Hospital is an independent risk-factor for suboptimal debulking compared to a similar population electively admitted to cytoreductive surgery, in a cohort of AOC patients treated at San Raffaele Hospital of Milan (Centre A);

ii) to validate the results identified in Centre A with similar patients in Centre B.

Patients and methods: This is a multicentre case-control study, analyzing a cohort of 111 and 196 AOC patients, treated at San Raffaele Hospital of Milan (Center A) and Gemelli Hospital of Rome (Center B) from January 2006/2008 to December 2010. Women are classified as patients admitted to the Hospital from ED (Cases) and out-patients (Controls).

Results: At univariate analysis, Cases significantly differ from Controls in terms of worse ECOG PS, larger ascites, pleuric effusion and peritoneal carcinomatosis. The rate of optimal cytoreduction is statistically lower in Cases than Controls. At multivariate analysis, significant independent predictors for suboptimal residual disease resulted ER admission, peritoneal carcinosis and mesenteral involvement,

Conclusions: Patients admitted from Emergency Department may have lower likelihood of optimal cytoreduction due to their poor clinical characteristics and diffusion of disease. This study identify a subgroup of AOC patients, the ones admitted from ER, who frequently do not appear in the reported largest series of women treated electively at Cancer Institutes without ED. In these women, intra-operative minimally invasive evaluation of the disease might help to discriminate if foregoing a more extensive surgery or neo-adjuvant chemotherapy.
Poster Session I

CYTOREDUCTIVE SURGERY PLUS HIPEC IN PLATINUM-SENSITIVE RECURRENT OVARIAN CANCER PATIENTS: A CASE-CONTROL STUDY ON SURVIVAL

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Objectives: To evaluate survival data in platinum sensitive recurrent ovarian cancer patients submitted to secondary cytoreduction (SCR) plus hyperthermic intraperitoneal chemotherapy (HIPEC) (Cases) compared to a group of women not experimenting HIPEC (Controls).

Materials and methods: Thirty Cases matched with 37 Controls, with at least 24 months of follow up, were retrospectively identified from a prospective database.

Results: Groups were comparable for all characteristics, except for a higher proportion of patients with single-nodule relapses in the Controls (19 vs. 6; p=0.011). Median follow up time was 46 months in the Cases and 36 months in the Controls. Twenty patients (66.6%) experienced secondary recurrence in the Cases and 37 women (100%) in the Controls (p=0.001). Moreover, 7 (23.3%) and 23 (62.2%) patients died of disease in the Cases and Controls respectively (p=0.003). The duration of secondary response was 26 months in the Cases and 15 months in the Controls (p=0.004).

Conclusions: The combination of SCR and HIPEC seems to improve survival rate in patients suffering from platinum-sensitive EOC recurrence with respect to no-HIPEC treatments. This result further supports the need of a randomized trial.
Poster Session I

A MULTI-CENTRIC TRIAL TO VALIDATE THE RELIABILITY OF A LAPAROSCOPIC SCORE TO ASSESS INTRAPERITONEAL DIFFUSION OF THE ADVANCED OVARIAN CANCER

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Purpose: To prospectively evaluate the agreement between tertiary referral centres in gynecologic oncology and the coordinator centre (CC) in performing a laparoscopic score to describe tumor spread in the advanced ovarian cancer (AOC).

Patients and methods: This is a prospective multi-centric trial. One hundred sixty-three patients with first clinical and/or radiological diagnosis of AOC were consecutively scheduled. The patients underwent staging-laparoscopy at the enrolling centre (EC) and the single laparoscopic parameters and overall score (PIV) were assessed and video-recorded. The accuracy of the laparoscopic evaluation at the EC was established through a blind revision of the videos by the CC. The minimum number of enrolling cases for each EC was 10 patients for 1 year, and an agreement of 80% was a priori established as an high-quality laparoscopic evaluation.

Results: Twenty-four centre participated to the study but only 17 of them (70.8%) enrolled patients. The definitive analysis was focused on the centres that enrolled at least 10 consecutive cases in 1 year. The median number of staging laparoscopies performed by each centre was 12 (range 10 - 13) and the median score was 6 (0 - 14) for EC and 4 (0 -14) for CC (p=ns). All centers overcome an overall agreement of 80% (range, 83.3% - 100%). The area under the ROC curve for the PIV of EC and CC ranged from 0.9 to 1.0 (p=ns).

Conclusions: The results suggest that the use of the laparoscopic score allows to reliably describe intraperitoneal diffusion of AOC among different centers.
Poster Session I

ELDERLY AND VERY ELDERLY ADVANCED OVARIAN CANCER PATIENTS: DOES THE AGE INFLUENCE THE SURGICAL MANAGEMENT?


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Background and aims: To examine the surgical treatment and clinical outcome of elderly and very elderly advanced epithelial ovarian cancer patients.

Methods: We retrospectively analyzed FIGO stage IIIC-IV ovarian cancer patients, divided in elderly (Group A, > 65 and < 75 years) and very elderly patients (Group B, ≥ 75 years) treated by primary debulking surgery (PDS) or by interval debulking surgery (IDS) at the Catholic University at Rome and Campobasso, Italy.

Results: 164 patients were included: 123 (Group A) and 41 (Group B). Complete cytoreduction was achieved in 60 patients (60.6%) in Group A and in 20 patients (62.5%) in Group B (p = 0.75). In the remaining cases, optimal cytoreduction was performed (39 cases (39.4%) in Group A and 12 (37.5%) in Group B; p = 0.75). In Group A complete/optimal debulking was achieved in 53 patients (53.5%) at PDS and in 46 patients (46.5%) at IDS (p = 0.55). In the Group B a higher rate of patients was debulked at IDS with respect to PDS (10 (31.3%) vs. 22 patients (68.7%); p = 0.02). In Group A patients debulked at PDS showed better DFS (p = 0.007) and OS (p = 0.003) than patients submitted to successful IDS, whereas in group B we did not observed any survival difference according to time of cytoreduction.

Conclusions: Our data suggest that elderly and very elderly patients may tolerate radical and ultra-radical surgery. These patients should be managed in a gynecologic oncology unit, with prudent but complete approach.
Poster Session I

BIOTINYLATED DENDRIMES NANO PARTICLES AS TARGETED SMVT RECEPTOR MEDIATED THERAPY FOR OVARIAN CANCER

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Worldwide, Ovarian cancer is the fourth most frequent cause of cancer death among women. It is considered as a chemo sensitive cancer. After clinically and surgically defined complete response to chemotherapy, the majority of women experience recurrence of the cancer within two years. These latter tumors generally do not respond to chemotherapy due to the development of drug resistance and spread into the peritoneal cavity resulting in the development of ascites. The emergence of nanotechnology has had a profound effect on development of therapeutic activity. Most chemotherapeutic agents have poor solubility and low bioavailability, and are formulated with toxic solvents. Thus, the use of nanoparticles allow for the preparation of low water soluble cancer medications in solid or liquid formulations. Dendrimers are a unique class of repeatedly branched polymeric macromolecules resulting in a nearly-perfect three-dimensional geometric pattern. Dendrimers for targeted delivery especially in cancer therapeutics has been shown to be effective. The multifunctional nature of the dendritic network makes it easier to incorporate both the drug and the targeting moieties simultaneously, and thus can be used for active targeting.

Targeting of tumors can also be achieved through PEGylation on the surface of dendrimers. On the surface of a variety of cancer cells, folate receptors are overexpressed. Folate-modified dendrimers target these cells via ligandreceptor recognition. Folic acid targeted dendrimers which are covalently conjugated with methotrexate specifically. Biotinylated dendrimers might be an effective nanoparticles which could be used both for antibody-based pretargeting and also SMVT receptor mediated targeting for ovarian cancer.
IMPACT OF ASCITES ON ANAESTHESIOLOGICAL AND SURGICAL OUTCOME OF PATIENTS WITH EPITHELIAL OVARIAN CANCER UNDERGOING EXTENSIVE CYTOREDUCTION

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Background: Cytoreductive surgery for epithelial ovarian cancer (EOC) is the worldwide accepted cornerstone in the clinical management of advanced ovarian cancer and is considered as high-risk surgery due to the incorporation of extensive multivisceral procedures. The additional challenge of fluid losses associated with the frequently presented ascites may deteriorate haemodynamic stability. There are no available data verifying the impact of ascites on perioperative management and outcome.

Methods: One hundred nineteen consecutive patients undergoing surgical cytoreduction in our institution due to EOC between 2005 and 2008 were included. The amount of ascites was determined at time of surgery and three groups were classified (no ascites[NOA,n=56], low amount of ascites[LAS,< 500ml,n=42], high amount of ascites[HAS,>500ml,n=21]).

Results: NOA compared to HAS showed less transfusions of red packed cells (0 vs.0 vs.3 units,p<0.001) and of fresh frozen plasma (0 vs.0 vs.2 units,p< 0.001). Additionally in patients with ascites noradrenaline was administered more frequently and in higher doses. Median length of stay in intensive care unit (ICU) was significantly shorter in NOA vs. LAS and HAS (1.0 vs.1.0 vs.3.0 days,p<0.001). Hospital length of stay was extended in HAS compared to patients without ascites (16 vs.17 vs.21 days,p=0.004). Postoperative complications were significantly increased in patients with ascites at the time of surgery (p=0.007).

Conclusions: The presence of high amount of ascites at cytoreductive surgery due to EOC is associated with higher amounts of blood-transfusions, while the length of hospital stay as well as the postoperative ICU treatment is significantly prolonged compared to abscence of ascites.
Poster Session I

BALANCED CRYSTALLOID VERSUS BALANCED COLLOID SOLUTION WITHIN A GOAL-DIRECTED HAEMODYNAMIC ALGORITHM IN PATIENTS UNDERGOING CYTOREDUCTIVE SURGERY DUE TO OVARIAN CANCER

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Background: In gynaecological surgery it is shown that intravenous fluid administration guided by haemodynamic monitoring reduced hospital length of stay and postoperative complication rates. This study compares a crystalloid and a colloid solution with respect to fluid requirements and side effects in multivisceral gynaecological surgery.

Methods: In a double-blinded pilot study, we randomly assigned 50 patients with primary ovarian cancer undergoing cytoreductive surgery to receive either balanced crystalloid or balanced starch solutions up to the dose limit (50ml/kgBW). The intraoperative administration of the study medication was yielded to optimize stroke volume measured by esophageal Doppler.

Results: Baseline patient characteristics were similar in both groups. There was no difference in FIGO classification, histological grades, intraoperative mapping of fields of tumour involved or the incidence of ascites between study groups. Without differences in heart rate, arterial or central-venous pressure the balanced starch solution maintained stroke volume better with administration of less study medication. Also, the patients in the colloid group reached dose limits of the study medication less frequently and later as well as required less transfusion of fresh frozen plasma units. Perioperative urine output and plasma levels of creatinine were equal in both study groups. No differences in the length of intensive care unit and hospital stay were found.

Conclusions: Within a goal-directed haemodynamic algorithm to optimize stroke volume a balanced HES solution is associated with better haemodynamic stability and minor need for fresh frozen plasma. There were no signs of impairment on renal function by colloid solutions in this study.
Poster Session I

EXPRESSION AND EPIGENETIC REGULATION OF ANGIogenesis RELATED FACTORS IN OVARIAN DORMANCY AND RECURRENCE MODEL IN VITRO

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Objective: To investigate the expression and epigenetic regulation of angiogenesis related factors in ovarian carcinoma dormancy and recurrence model in vitro.

Methods: The inducible Tet-on SKOV3-ARHI ovarian carcinoma cell line was used. The in vitro ovarian carcinoma dormancy and recurrence model was established by doxycycline maintenance and withdrawal in combination with vascular epithelial growth factor (VEGF) treatment. Cell growth and proliferation were measured by colony formation assay. Expression and methylation of angiogenesis related factors with or without 5-aza-2'-deoxycytidine (5-aza-dC) and trichostatin A (TSA) treatment were detected by real-time PCR and bisulfate sequencing.

Results: The in vitro ovarian carcinoma dormancy and recurrence model was successfully established. Among 15 genes studied, 6 genes' expression was up-regulated in dormancy and down regulated in recurrence and methylation level of three genes (tissue inhibitor of metalloproteinases 3, TIMP-3; Thrombospondin 1, TSP1; E-cadherin, CDH1) was higher in recurrence compared with dormancy. After 5-aza-dC treatment in the recurrence group, nine genes' expression was restored. In agreement with increased expression, methylation level of 3 genes (TIMP3, TSP1, CDH1) was down-regulated by 5-aza-dC. Five genes’ expression increased after TSA treatment. The colony formation ability was inhibited significantly after 5'-aza-dC and/or TSA treatment in recurrent group.

Conclusion: Angiogenesis related factors that regulated by methylation played a key role in ovarian carcinoma dormancy to recurrence transition. DNA methyltransferase and histone deacetylase inhibitors could restore the expression of the angiogenesis inhibitory factors such as TIMP-3, TSP-1 and CDH1 thus reverse the process of recurrence.
Poster Session I

RISK-REDUCING SALPINGECTOMY IN LOW RISK PATIENTS: ASSESSING THE IMPACT OF A NOVEL REQUEST FOR SURGICAL PRACTICE CHANGE

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Introduction: In September 2010, BC’s ovarian cancer research group sent an educational package to BC gynecologists outlining the evidence for the fallopian tube (FT) site of origin for the majority of ovarian high grade serous carcinomas (HGS) and the association of BRCA1/2 mutations with HGS. Gynecologists were asked to consider removal of FT at the time of hysterectomy and in lieu of tubal ligation. We wished to measure the uptake of and barriers to this surgical practice change.

Methods: 206 surveys were electronically distributed to BC gynecologists (Zoomerang).

Results: Of 110 respondents (53%) 70% were general OB/GYN, and 70% practicing > 10 years. 79% correctly identified the tubal epithelium as the site of origin of HGS and cancer prevention was the primary reason for recommending salpingectomy (82%). 82% stated they always or mostly recommended salpingectomy at the time of hysterectomy and 75% would NOT have considered this prior to the 2010 BC recommendations. Tubal ligation recommendation was lower at 50%. Top reasons cited for NOT recommending salpingectomy included concern for complications, and the increased time required to counsel patients. Of note, 56-58% of respondents felt there were NO barriers to implementation. 62% described themselves as rapid/relatively rapid adaptors of new innovations/techniques. Going forward, published guidelines by the SOGC/GOC would hold the greatest weight in influencing their practice (84%).

Conclusions: Surgical practice change among BC gynecologists is very encouraging. Data on costs and complications are forthcoming and should provide reassurance, promoting greater uptake in BC and in any center considering adoption of these recommendations.
Poster Session I

SUPPORTIVE CARE NEEDS OF OVARIAN CANCER PATIENTS

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Women diagnosed with ovarian cancer may experience many short-term and long-term effects from cancer and its treatment. Cancer has more than a physical impact, yet there is a lack of information about the types of needs these women have and whether they want help in meeting their needs.

The main purpose of this cross-sectional descriptive study was to identify the supportive care needs (physical, social, emotional, informational, spiritual, psychological and practical) of women with ovarian cancer who attended a comprehensive outpatient cancer centre. A further purpose was to determine if women wanted assistance in meeting those needs.

A total of 50 women diagnosed with ovarian cancer participated in this study by completing a self-report questionnaire (The Supportive Care Needs Survey).

The data indicated that a range of supportive care needs remained unmet for this patient group. Eight of the top 10 most frequently reported needs were psychosocial, such as fears about the cancer returning or spreading. The women also expressed a range of difficulty in managing physical and psychosocial needs. However, despite this reality significant numbers of women indicated they did not wish to have assistance from the clinic staff with some unmet needs.

Women diagnosed with ovarian cancer have unmet physical and psychosocial needs. Tailored assessment and intervention are required to meet these individualized needs. Suggestions for practice and future research are offered to assist in providing care to these women.
Poster Session I

CLINICAL OUTCOME OF EN-BLOC INTESTINAL RESECTIONS IN THE PALLIATIVE SETTING OF HIGHLY ADVANCED OVARIAN CANCER

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Background and aims: Salvage surgery for patients with highly advanced forms of OC complicated by severe events such as bowel obstruction or intestinal perforation constitutes a therapeutic dilemma. Our aim was to evaluate surgical and clinical outcome after such “limit”-procedures.

Methods: We evaluated EOC-patients who underwent salvage extraperitoneal en bloc intestinal resection with terminal ileo-/jejunostomy resulting in short-bowel-syndrome (SWS) and whole-life total-parenteral-nutrition between 05/2003 and 01/2012 in our institution.

Results: Forty-four patients were identified (median age: 58y; range: 22-75); 5 (11.4%) with primary- and 38 (86.4%) with relapsed-OC. Five (11.4%) patients were platinum-sensitive; 7 (16%) were pretreated with bevacizumab. Indications for surgery were bowel obstruction (86.4%), spontaneous intestinal perforation (6.9%) and intestinal fistula (4.6%). Median residual intestinal length was 70cm (range:10-180cm); 25 (56.8%) patients had a residual intestinal length < 1cm. In 8 (18.2%) patients optimal tumor residuals (0-0.5cm) could be obtained. Operative 30-days-mortality and major morbidity rates were 9% and 50%, respectively. Median overall-survival was 5.4months (range:0-49). 1-year-OS rate was 20.1% (95% CI:7.7-32.6). Within a median follow up period of 5 months (range:0.2-49) only 4(9.1%) patients are still alive. No significant differences in survival were seen between patients with or without major complications, tumor residuals or residual intestinal length of < 1m versus >1m. Previous treatment with bevacizumab did not affect outcome or operative morbidity.

Conclusions: Salvage surgery due to severe intestinal complications in advanced OC are associated with high operative morbidity, however a considerable prolongation of survival in a life-threatening situation. Indication for such surgeries should be set with caution.
Poster Session I

EVALUATION OF BRCA1 GENE EXPRESSION AS A PROGNOSTIC MARKER IN PERITONEAL CANCER

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\textbf{Purpose:} BRCA1 gene dysfunction seems to be present in up to 50\% of patients with sporadic ovarian cancer, and lower BRCA1 expression is correlated with better overall survival (OS). Peritoneal cancer has a worse prognosis than ovarian cancer. The aim of the present retrospective study was to evaluate the correlation between the frequency of BRCA1 gene dysfunction, clinical data, and overall survival.

\textbf{Materials and methods:} We retrospectively evaluated 14 patients diagnosed with serous peritoneal cancer (all stage IIIC), other than hereditary breast and ovarian cancer, between 2005 and 2010. All patients had serum CA125 levels >40 IU/mL prior to starting first-line chemotherapy with paclitaxel and carboplatin. BRCA1 and p53 protein expression was determined by immunohistochemistry of patient tissue samples. The Cox proportional hazards model was used to calculate the significant factors contributing to OS.

\textbf{Results:} Only the CA125 regression rate from two initially elevated samples were significantly correlated with OS. High BRCA1 expression was detected by immunohistochemistry in 9 (64\%) patients, which had a median survival of 22 months (range, 2-82). Low BRCA expression was detected 5 (36\%) patients, which had a median survival of 35 months (range, 11-72).

\textbf{Conclusions:} The findings of the present study suggest that prognosis of serous peritoneal cancer correlates with the CA125 regression rate. In addition, low BRCA1 gene expression was detected by immunohistochemistry in 36\% of patients with peritoneal cancer and leads to a better prognosis than high BRCA gene expression.
Poster Session I

OVARIAN SEX CORD STROMAL TUMORS: A CLINICAL REVIEW WITH A LONG-TERM FOLLOW-UP OF 338 CASES

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The aim of the present study was to describe the surgical and clinical outcomes of SCSTs of the ovary with a long-term follow-up. All medical records of patients with SCSTs of the ovary that were managed as in- or outpatients, in two Institutions between 1981 and 2011, were reviewed. We found a total of 338 patients (pts) with a median age at diagnosis of 43 years (4-82 years). Two hundred forty-three (72%) pts had adult granulosa cell tumor, 39 (12%) juvenile granulosa cell tumor and 56 (16%) Sertoli-Leydig cell tumor. Three hundred five (89%) pts had stage I, 12 (4%) stage II, 33 (6%) stage III. Endometrial biopsy was performed in 70% of the pts: endometrial hyperplasia was found in 47 and endometrial cancer in 7 pts. The tumor median size was 109 mm (range 4-370 mm). Considering all stages, fertility-sparing surgery was performed in 185 pts (55%). Adjuvant platinum-based chemotherapy was administrated in 59 pts (42% early stage; 58% advanced stage). During a median follow-up period of 132 months (2-411 months), 44 (13%) died for the progression of disease. Relapses occurred in 67 early stage pts (21%). Median time to recurrence was 62 months (5-303 months). In this group there was no difference about relapses between laparoscopy (18%) and laparotomy (16%). Our series confirms the excellent prognosis of SCSTs. In young patients, fertility sparing surgery should be always attempted and laparoscopic approach should be considered. Due to the long time to recurrence, these pts require a long term follow up.
NOMOGRAM FOR 30-DAY MORBIDITY AFTER PRIMARY CYTOREDUCTIVE SURGERY FOR ADVANCED STAGE OVARIAN CANCER

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Objectives: Extensive surgical procedures to achieve maximal cytoreduction in patients with advanced stage epithelial ovarian cancer (EOC) are inevitably associated with postoperative morbidity and mortality. The current study aims to identify preoperative predictors of 30-day morbidity after primary cytoreductive surgery for advanced stage EOC and to develop a nomogram for individual risk assessment.

Materials and methods: All patients in the South Western part of the Netherlands who underwent primary cytoreductive surgery for advanced stage EOC between January 2004 and December 2007 were identified from the Rotterdam Cancer Registry database. All peri- and postoperative complications within 30 days after surgery were registered and classified according to the definitions of the National Surgical Quality Improvement Program (NSQIP).

To investigate independent predictors of 30-day morbidity, a Cox’ proportional hazard model with backward stepwise elimination was utilized. The identified predictors were entered into a nomogram.

Results: Two hundred ninety-three patients entered the study protocol. Optimal cytoreduction was achieved in 136 (46%) patients. 30-day morbidity was seen in 99 (34%) patients. Morbidity could be predicted by age ($P = 0.033$; OR 1.024), haemoglobin ($P = 0.194$; OR 0.843) and WHO performance status ($P= 0.015$; OR 1.821) with a for optimism corrected c-statistic of 0.62.

Conclusions: 30-day morbidity could be predicted by age, haemoglobin and WHO performance status. The generated nomogram could be valuable for predicting operative risk in the individual patient.
Poster Session I

ROLE OF APPROPRIATE SURGERY IN SURVIVAL OF PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Background and aim: Management of epithelial ovarian cancer (EOC) patients is largely based on appropriate surgery. The principle treatment of early stage is competence of surgical staging surgery and surgical management of all patients with advance EOC is approach in a similar manner with cytoreduction surgery. We decided to evaluate the impact of appropriate surgery as a scale on 2 and 5-year survival in EOC patients.

Methods: In a descriptive analytic study a total 186 patients were divided into 62 with early stage of EOC equivocal FIGO stage I and 124 with advanced disease at Vali-e-Asr Hospital affiliated with Tehran University of Medical Science, Iran, from 1998 to 2008. Two and 5-year disease free survival (DFS) and overall survival rates were determined and compared between the two groups using chi-squared test, Kaplan Meier and Cox regression.

Results: Five-year DFS in patients with early stage of disease was 85% for the surgical staging group and 38% for non-surgical staging group (P=0.037). Two-year DFS and overall survival did not differ between the groups. Also 5-year survival rates in subjects with surgical staging surgery were 42% and 40% for non staging group. For patients assigned to advanced disease group, 5-year DFS in subjects with cytoreductive surgery was 73% and the figure for the remainder was 58%. Five-year overall survival rate in cytoreductive surgery group was 43% in comparison to 38% in the second group.

Conclusions: Maximal effort for appropriate surgery appears to be a corner stone for optimal survival.
INCIDENCE OF OVARIAN CLEAR CELL CARCINOMA IN ASIAN AND NORTH AMERICAN POPULATIONS

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Background: Clear cell carcinoma is an uncommon subtype of ovarian carcinoma and is widely believed to be more common in Asia, compared to North America or Europe. The aim of this study was to compare the incidence of clear cell carcinoma in Singapore, Taiwan, and British Columbia, Canada, based on recently diagnosed cases.

Design: Tumor registry data was used to identify cases of clear cell carcinoma in Singapore (during the period 1993-2007), Taiwan (1994-2008), and British Columbia (1993-2008). The percentage of all recorded cases of ovarian carcinoma that were of clear cell type was determined, as was the incidence per 100,000 population.

Results: 387, 1163, and 548 cases of clear cell carcinoma were identified in the tumor registries of Singapore, Taiwan, and British Columbia, respectively. Clear cell carcinomas accounted for 19.1% (Singapore), 15.3% (Taiwan), and 10.2% (British Columbia) of cases of ovarian carcinoma. The incidence of clear cell carcinoma of the ovary was as follows: Singapore - 0.651/100,000; Taiwan - 0.709/100,000; British Columbia - 0.796/100,000.

Conclusions: Although clear cell carcinomas were relatively more common in Singapore and Taiwan, compared to British Columbia, the incidence was similar, suggesting that clear cell carcinomas may only be relatively more common in Singapore and Taiwan, compared to other ovarian carcinoma subtypes, rather than more common in absolute terms. Thus, the perception that ovarian clear cell carcinoma is more common in Asian populations may reflect other ovarian carcinoma subtypes being less common, rather than there being an increased incidence of clear cell carcinoma.
Poster Session I

DOSE-DENSE PACLITAXEL WITH CARBOPLATIN FOR ADVANCED OVARIAN CANCER: A FEASIBLE TREATMENT ALTERNATIVE

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Objective: Epithelial ovarian cancer is the leading cause of death from gynecologic cancers in the Western world. If possible, initial cytoreductive surgery is the treatment of choice, followed by adjuvant chemotherapy, usually with a platinum/taxane combination. Increased survival has been recently reported in women who were given weekly adjuvant chemotherapy rather than at standard three week intervals. At the Tom Baker Cancer Centre in Calgary, Canada, we have been treating patients with advanced ovarian cancer with a dose-dense protocol since March 2010. Treatment was given in an outpatient setting on Days 1, 8 and 15 of a 21-day cycle for six cycles. Carboplatin AUC 5 mg/mL and paclitaxel 80mg/m² were given on day 1, followed by paclitaxel 80mg/m² on days 8 and 15. Our objective was to determine if this protocol was achievable at our centre.

Patients and methods: We performed a chart review of 46 patients undergoing treatment with dose-dense chemotherapy for advanced ovarian cancer. Demographic information, patient characteristics, adverse events, and treatment endpoints were recorded.

Results: Sixty-one percent of women completed the six-cycle protocol as planned with minimal interruption, which is comparable to the only trial using this regimen. The most common side effects of treatment were fatigue, neuropathy, and neutropenia. Supplementation with regular magnesium and granulocyte colony-stimulating factor reduced delays.

Conclusion: Dose-dense paclitaxel with carboplatin chemotherapy for the treatment of advanced ovarian cancer shows promise in terms of progression-free and overall survival. We have shown this protocol to be practical and feasible in our population.
Poster Session I

TYPE-SPECIFIC RESPONSE TO NEOADJUVANT CHEMOTHERAPY: OVARIAN HIGH-GRADE SEROUS CARCINOMAS VERSUS COLORECTAL MUCINOUS CARCINOMA

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Introduction: Ovarian carcinomas are currently managed as a single entity with no stratification for histological type. The foundation of treatment is a combination of surgery and chemotherapy. Women that are not candidates for up-front debulking surgery, either because of performance status or widespread disease are often offered neoadjuvant chemotherapy in an effort to shrink their tumours and make resection possible.

By far the most common type of ovarian carcinoma is high-grade serous carcinoma, accounting for two thirds of cases. Less common types are clear cell (12%), endometrioid (10%), mucinous (3%) and low-grade serous (3%) carcinomas. Although high-grade serous carcinomas are usually initially exquisitely chemosensitive, other types seem to show a much lower response rate. Recent improvements in histological classification allow a highly reproducible diagnosis based on morphology alone or with the use of ancillary immunohistochemistry.

Case report: A 76 year old woman was treated with neoadjuvant platinum-based chemotherapy for advanced ovarian cancer. At interval debulking surgery, she was found to have a concurrent mucinous colorectal carcinoma that was essentially untouched by her treatment.

Conclusion: This case serves as an in-vivo demonstration of the resistance of mucinous carcinomas to platinum-based treatments, compared to high-grade serous, the 'typical' ovarian cancer.

Reproducible diagnosis sets the foundation for type-specific management. It has been suggested that mucinous ovarian tumours be treated differently, possibly similarly to colorectal carcinomas. A more stratified approach will potentially yield better treatment alternatives for rare or 'special' types.
Poster Session I

FIRST EFFICACY RESULTS FROM OCTAVIA: FRONT-LINE BEVACIZUMAB (BEV) COMBINED WITH WEEKLY PACLITAXEL (WPAC) AND Q3W CARBOPLATIN FOR OVARIAN CANCER


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Background: BEV given with front-line chemotherapy (q3w PAC + q3w carboplatin) followed by BEV alone significantly improved progression-free survival (PFS) vs chemotherapy alone in the GOG-0218 and ICON7 randomised phase III trials in ovarian cancer (OC). The single-arm OCTAVIA study evaluated front-line BEV + wPAC + q3w carboplatin. Safety results have been presented previously. Here we report final PFS and additional secondary efficacy results.

Methods: Patients with newly diagnosed OC (stage Iib-IV or high-risk stage I-IIa) received BEV (7.5 mg/kg, d1) + WPAC (80 mg/m² d1, 8, 15) + carboplatin (AUC6, d1) iv q3w for 6-8 cycles, followed by single-agent BEV q3w for up to 17 cycles (1 year) in total. The trial was designed to recruit a patient population similar to that in ICON7. The primary endpoint was PFS. Secondary endpoints included response rate, duration of response, overall survival and safety.

Results: Between Jun 2009 and Jun 2010, 189 eligible patients were enrolled (median age 55 years [range 24-79]; 74% ECOG 0; 80% stage III/IV; 65% serous; 71% optimally debulked). Patients received a median of 6 chemotherapy cycles and 17 BEV cycles. At the data cut-off (XX June 2012), disease had progressed in XX pts (YY%) and AA (BB%) had died. Median PFS was XX months (95% CI: YY—ZZ). [PFS in key subgroups may be included]. The response rate was YY%. OS data are immature. The regimen was tolerable with a safety profile consistent with the well-defined profile in phase III OC trials.

Conclusions: [To be added]
Poster Session I

MALIGNANT OVARIAN GERM CELL TUMORS: TREATMENT AND FAILURE TREATMENT ASSESSMENT

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Introduction: Malignant Ovarian Germ Cell Tumors (MOGCTs) are more common in Asian (15%) vs Western countries (5%).

Objective: This study was done to review all patients with MOGCTs who were diagnosed and treated in our institute or referred from other hospitals for post surgical treatment.

Aims: The aims of the study were evaluation of clinicopathologic characteristics, long-term outcome and prognostic factors for treatment failure (TF), which was considered as death or recurrence.

Patients and methods: In this retrospective study, 150 patients with MOGCTs during 1996-2011 were assessed. After evaluating the patients’ files, data were entered and analyzed by SPSS software. Descriptive statistics, chi-square, Man-Whitney and survival analysis tests were used.

Results: The mean age of patients and follow-up duration was 23.33 (11-60, SD=8.864) and 46.98 (1-180, SD= 35.372) respectively. 55 (36.7%) patients were primarily treated in our department whose 10-year-survival rate 92%, while 95 (63.3%) patients were referred from non academic centers after surgery with 77% 10-year-survival rate. The majority of patients had unknown primary stage (39.2%, n=58). The most common histology type and chemotherapy regimen were dysgerminoma (35.5%, n=54) and BEP (90/3%) respectively. Significant associations were seen between patient age (p=0.044), suboptimal surgery (p< 0.001), tumor histological type (p= 0.003), first treatment place (p=0.003), disease stage and TF. There was no relation between tumor size and TF.

Conclusion: MOGCTs are curative tumors if they treat properly or at an academic specialized center. Appropriate first surgical approach, prevention of tumor spillage, precise pathologic report and rapid onset of chemotherapy in the case of necessity, provide long term survival with fertility preservation in these patients.
Poster Session I

ANALYSIS ON THE EXPRESSION OF BDNF AND ITS RECEPTOR TRKB IN OVARIAN CANCERS

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Objectives: BDNF/TrkB signal promotes cell survival and differentiation through tyrosine kinase (TK) domain. Two types of TrkB molecular structure were identified; full length type with intracellular TK domain and truncated type without the TK domain. In this study, we focused on the relation of BDNF/TrkB expressions in ovarian cancers to examine if any atypical signal pathway exists in ovarian cancers.

Methods: Samples of ovarian cancers\((n=105)\), endometriums\((n=27)\), endometriosis\((n=17)\) and ovarian benign tumors\((n=9)\) were obtained from patients who underwent surgery in Tokai University Hospital from 1994 to 2010 with informed consent. Samples contained mucinous\((n=11)\), serous\((n=19)\), endometrioid\((n=25)\) and clear cell\((n=50)\) adenocarcinomas. The sections of formalin-fixed, paraffin-embedded samples were stained with two polyclonal antibodies against extracellular domain and TK domain of TrkB and a monoclonal antibody against BDNF. RT-PCR was performed using total RNA extracted from frozen samples of ovarian cancers; mucinous\((n=3)\), serous\((n=3)\), endometrioid\((n=3)\) and clear cell\((n=16)\) adenocarcinomas and various primers for BDNF and TrkB variants.

Results: The ratio of TrkB positive cases in ovarian cancers was significantly high with 75.2% \((P<0.05)\). Among TrkB positive cases, the ratio of full length type was 17.8%. The ratio of BDNF positive cases in ovarian cancers was 83.8%. BDNF/TrkB was also expressed in ovarian cancers in mRNA level. More than 50% of clear cell adenocarcinomas expressed TrkB variant which has defect in exon 9-12 where BDNF binding site is involved.
Poster Session I

ACCURACY AND REPRODUCIBILITY OF THE PERITONEAL CANCER INDEX IN ADVANCED OVARIAN CANCER IN LAPAROSCOPY AND LAPAROTOMY

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Objective: The aim of this prospective study were to evaluate the accuracy of the Peritoneal Cancer Index (PCI) between laparoscopy and laparotomy and to evaluate the reproducibility of this index between 2 observers in advanced stage ovarian cancer (ASOC).

Summary background data: In ASOC the quality of the cytoreductive surgery, which is the main prognosis, is correlated with the extension of the disease and so with the PCI. The reliability of this scoring index between different surgeons in laparoscopy and laparotomy has not yet been studied in this disease.

Methods: Between April 2010 and October 2011, for each of the 29 patients undergoing complete cytoreductive surgery, one senior surgeon and one junior surgeon evaluated the PCI score at 3 times the same day: during laparoscopy and during laparotomy at the beginning and at the end. A concordance analysis was conducted with Bland and Altman’s method and estimated by intraclass correlation coefficients.

Results: There was a high concordance of the PCI score between junior and senior surgeons in laparoscopy and laparotomy: the mean differences were not significantly different from zero (p< 0.05) and 95% limits of agreements were +/- 3.5 and +/- 3.0 respectively. Laparoscopic underestimated the PCI score of 2 points approximately compared to the beginning of the laparotomy: mean biases were -2.0 (95%CI -2.8, -1.2) for the senior surgeon and -2.2 (95%CI -3.1, 1.3) for the junior.

Conclusion: The PCI score is reproducible and reliable, to evaluate the peritoneal spread in ASOC.
Poster Session I

PROGNOSTIC VALUE OF PREOPERATIVE GAMMA-GLUTAMYLTRANSFERASE (GGT) SERUM LEVELS IN PATIENTS WITH OVARIAN CANCER

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Background and aim: Gamma-Glutamyltransferase (GGT) is a membrane-bound enzyme, which is crucially involved in the cell’s anti-oxidative pathway. GGT has also been described to be involved in the carcinogenesis of solid tumors. Increased GGT serum levels have been reported to be associated with an increased risk and worse prognosis for a variety of gynecologic cancers. The aim of the study was to investigate the association between preoperative GGT serum levels and survival in patients with epithelial ovarian cancer (EOC).

Methods: The present multicenter study comprised 634 consecutive patients (567 with ovarian cancer, 67 patients with borderline tumor of the ovary [BTO]) of two prospectively maintained cancer registries at the Medical University of Vienna and Innsbruck, Austria. Preoperative GGT serum levels between EOC and BTO patients were compared. EOC patients were stratified in four previously described GGT risk groups (group A: GGT< 18 U/l, group B: GGT 18-35.99 U/l, group C: 36.00-71.99 U/l, group D: >72.00 U/l) and their prognostic values were calculated by log-rank tests and Cox-regression models.

Results: Mean preoperative GGT serum levels were significantly elevated in EOC patients (28.6 [38.2] U/l) compared to BTO patients (20.0 [12.8] U/l) (p=0.01). EOC patients with elevated GGT serum levels had a shorter overall survival in univariate (p=0.004) and multivariate analysis (HR 1.2 [1.0-1.5]; p=0.03).

Conclusions: Patients with EOC had higher preoperative GGT serum levels than patients with BTO. In patients with EOC, elevated GGT serum levels were independently associated with shorter overall survival.
Poster Session I

OVARIAN CANCER IN TURKEY

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Objective: To compare ovarian cancer incidence in Turkey and in the world.

Method: Cancer registry begun in 1992 in Turkey and it has gained momentum with serial international registry trainings. Data stream to be provided from government hospitals, university hospitals, private hospitals, private policlinics and laboratories from the eight provinces that were included active registry system. This data had been written in Can-Reg 4 Program, after the quality controls done and incidence was calculated per year.

Results: According to 2008 data, ovarian cancer was among the first five common cancers in females. The incidence of ovarian cancer in 2002-2008 period was between 5.6 and 6.5; with an average of 6.0 per 100,000 cases (SD: 0.3; 95% CI 5.41-6.59). Ovarian cancer incidence of European countries (EU27) was higher than Turkey. On the other hand the incidence of Turkey was similar to the rest of the world which was 6.3 per 100,000 according to Globocan 2008 data. The distribution of cancer stage was also similar to the world literature just in that way; 31.5% of disease was diagnosed in early stages while 68.5% diagnosed at late stages.

Conclusion: Ovarian cancer epidemiology of Turkey is found to be similar to the other developing countries in the world.
Poster Session I

PELVIC ACTINOMYCOSIS: A DISEASE THAT SHOULD NOT BE OVERLOOKED IN CASES WITH SUSPECTED ADVANCED OVARIAN CANCER

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Introduction: Pelvic actinomycosis (PA) is a chronic granulomatous infection caused by gram-positive anaerobic bacilli, Actinomyces israelii. The indolent clinical course and malignant appearing features in imaging studies such as presence of ascites, nodular implants and abdominal pelvic masses generally cause a diagnostic challenge for the clinicians. Herein we present a case of PA mimicking an advanced ovarian cancer, who was diagnosed and treated at a gynecologic oncology unit of a tertiary medical care center.

Case: A 51 year-old woman, who had a copper IUD for the last 17 years, applied to our institution complaining of pelvic pain, abdominal distention, weight loss and vaginal discharge. She had elevated serum levels of CA-125 (75 U/ml) and bilateral multiloculated cystic masses with solid components measuring 51x45 mm and 65x47 mm in the right and left iliac fossae (Figure 1), respectively, which caused bilateral hydronephrosis (Figure 2). Exploratory laparotomy revealed partially necrotic and hemorrhagic bilateral solid cystic pelvic masses, which were reported as benign on frozen section. Total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. Final histopathologic examination confirmed a definitive diagnosis of bilateral salpingo-ovarian actinomycosis, which showed actinomycyes (sulfur) granules (Figure 3). The patient received intravenous penicillin G for 2 weeks followed by oral penicillin for additional 6 months. Post-treatment follow-up was uneventful.
[Figure 2]
Conclusion: The clinical presentation of PA is very similar to pelvic malignancies. This may cause these patients to be referred to gynecologic oncologists for primary treatment. PA should be included in differential diagnosis of infiltrating intra-abdominal disorders, especially in reproductive women with IUD in situ.
CLINICAL ANALYSIS OF PRIMARY FALLOPIAN TUBE CANCER CASES WITHIN A FIVE YEAR PERIOD: A SINGLE CENTER EXPERIENCE IN ANKARA, TURKEY

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Aims: To analyze primary fallopian tube cancer (PFTC) cases which were diagnosed and treated in gynecologic oncology department of a tertiary hospital in Ankara, Turkey.

Methods: Hospital cancer registry database was reviewed for PFTC between January 2006 and January 2011. Data regarding patient age, menopausal status, presenting symptom, serum CA-125 level, tumor size, tumor histology and disease stage were analyzed.

Results: Eighteen PFTC cases were identified. Mean patient age was 57.7±8 (min44-max70). Mean tumor size was 90±39.9mm (min24-max168). Fourteen case (%77.8) were postmenopausal. Four cases (22.2%) were asymptomatic at the time of diagnosis. Ten cases (55.6%) presented with pelvic pain, 2 cases (11.1%) presented with abdominal distention, 2 cases (11.1%) presented with postmenopausal bleeding. Eleven cases (61.1%) had elevated serum CA125 levels at diagnosis. Fourteen cases (77.8%) had serous, 2 cases (11.1%) had endometrioid, 1 case (5.6) had clear cell adenocarcinoma, and 1 case (5.6%) had sarcoma. Seven cases (38.9%) had FIGO stage-I, 5 cases(27.8%) had stage-II, and 6 cases(33.3) had stage-III disease.

Conclusions: Our data indicate similar findings with the literature. PFTC is a rare gynecologic malignancy, which follows a parallel clinical course with epithelial ovarian cancer (EOC). Papillary serous histology is common in these tumors. Accurate pathological diagnosis of PFTC may be challenging in these cases, as the tubal site is very close to the ipsilateral ovary, and histopathological characteristics closely resemble EOC. Although there are no prospective randomized trials, currently recommended primary treatment consists of optimal cytoreduction and adjuvant platinum based chemotherapy.
Poster Session I

CLINICAL ANALYSIS OF OVARIAN GRANULOSA CELL TUMOR CASES OVER A FIVE YEAR PERIOD: A SINGLE CENTER EXPERIENCE IN ANKARA, TURKEY

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Aim: To analyze cases with adult type granulosa cell tumors (GCT) of the ovary, which were treated in gynecologic oncology department of a tertiary referral hospital in Ankara, Turkey.

Methods: Hospital database was reviewed for GCT cases treated between January 2007 and January 2012. Data regarding patient age, menopausal status, presenting symptom, preoperative endometrial status, serum CA-125 level, type of surgery, disease stage, retroperitoneal lymph node metastasis (RLNM) and peritoneal tumor involvement (PTI) were analyzed.

Results: A total of 40 GCT cases were identified. Mean patient age was 51.2±8.1 years. Majority of the patients(77.5%) were younger than 60 years of age. Eighteen cases(45%) were premenopausal and 22 cases(55%) were postmenopausal. Seven cases(17.5%) were asymptomatic at the time of diagnosis. Eighteen cases(45%) presented with abnormal uterine bleeding, 14 cases(35%) with pelvic pain and one case(2.5%) with acute abdomen. Twelve cases(30%) had normal endometrial biopsy, 26 cases(65%) had endometrial hyperplasia and two cases(5%) had endometrial cancer. Preoperative CA125 levels were elevated(>35U/ml) in 13 cases(32.5%). Seventy percent of the cases had FIGO stage I-II disease. Four cases(10%) were treated with fertility preserving surgery. Four cases(10%) had PTI and 5 cases(12.5%) had RLNM.

Conclusions: GCT of the ovary is a rare gynecologic malignancy which comprises 2-5% of all ovarian cancers. Most cases present at early stages and surgical treatment is generally sufficient. Fertility sparing surgery is also an acceptable approach for young women desiring future fertility. Endometrial evaluation with biopsy is especially important in cases with GCT, as concomitant endometrial pathologies are very common.
Poster Session I

GASTROINTESTINAL MALIGNANCIES RESEMBLING ADVANCED OVARIAN CANCER: A SINGLE CENTER EXPERIENCE IN ANKARA, TURKEY

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Aim: To analyze cases with gastrointestinal system (GIS) cancers, which primarily presented with clinical features resembling advanced ovarian cancer. All of the cases were treated in the gynecologic oncology department of a tertiary referral hospital in Ankara, Turkey.

Methods: Patient database was reviewed for GIS cancer cases treated in our gynecologic oncology department between January 2007 and January 2012.

Results: A total of 28 GIS cancer cases were identified. Mean patient age was 48.6±13.7 years (minimum 24, maximum 73). Eleven cases (39.3%) presented with gastrointestinal symptoms such as nausea, vomiting and early satiety. Six cases (21.4%) presented with abdominal pain, 5 cases (17.9%) with adnexal mass and 3 cases (10.7%) with abdominal distention. Serum CA125 levels were elevated in 19 cases (67.9%) and CA19-9 levels were elevated in 18 cases (64.3%). Thirteen cases (46.4%) were premenopausal and 15 cases (54.6%) were postmenopausal. Final pathology was reported as colon cancer in 10 cases (35.7%), gastric cancer in 8 cases (28.6%), appendiceal cancer in 5 cases (17.9%), small bowel cancer in 4 cases (14.3%) and rectum cancer in 1 case (3.6%).

Conclusions: GIS malignancies may occasionally mimic advanced ovarian cancer in terms of clinical, radiological and laboratory findings. Initial surgical procedures in these cases may be performed by gynecologic oncologists as a consequence of this resemblance. GIS origin should be suspected, especially in cases with prominent gastrointestinal symptoms and CA19-9 elevation. Perioperative consultation with a gastrointestinal surgeon is warranted in these cases.
Poster Session I

PRIMARY TUMORS OF THE APPENDIX MIMICKING ADVANCED OVARIAN CANCER: REPORT OF FIVE CASES FROM ANKARA, TURKEY

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Introduction: Appendiceal tumors account for less than 0.5% of all gastrointestinal neoplasms and among these, mucinous adenocarcinoma is the most common histological type. Most cases of pseudomyxoma peritonei (PMP) are reported to be caused by low-grade mucinous appendiceal tumors.

Case report: We present five cases of primary appendiceal tumor, which were diagnosed and treated in a tertiary referral hospital in Ankara, Turkey between June 2009 and February 2012. All of the cases were referred to our hospital's gynecologic oncology department for evaluation of a pelvic mass highly suspicious for advanced ovarian cancer. Final diagnosis in these cases could be established only after exploratory laparotomy. The clinicopathological presentation of these cases were metastatic low grade mucinous neoplasm of appendix with pseudomyxoma peritonei, insular type carcinoid tumor of the appendix along with borderline serous tumor of the right ovary, moderately differentiated appendiceal mucinous adenocarcinoma, metastatic undifferentiated appendiceal mucinous adenocarcinoma, and metastatic appendiceal mucinous adenocarcinoma . All cases underwent a complete cytoreductive procedure including appendectomy, hysterectomy , bilateral salpingo-oophorectomy, omentectomy , bilateral pelvic and paraaortic lymphadenectomy and debulking of tumoral masses.

Discussion: Appendiceal malignancies are often associated with an atypical presentation, thus creating diagnostic challenges for clinicians and pathologists. Not infrequently, definitive diagnosis is only possible after surgical exploration. A multidisciplinary treatment approach is warranted in these cases, with collaboration between departments of gynecologic oncology, gastrointestinal surgery and medical oncology.
Poster Session I

RARE OVARIAN TUMORS- A SINGLE CENTER EXPERIENCE OF 15 YEARS

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Objective: The present study aims to review cases of extremely rare primary ovarian tumors and thus, to evaluate the distribution of rare primary ovarian pathologies.

Methods: A retrospective review of women, with final pathology of rare primary ovarian tumors, which were managed at the Gynecologic Oncology Department of Zekai Tahir Burak Women’s Health Education and Research Hospital, from 1995 to 2010 was undertaken.

Results: Among the 2210 women treated during the study period, extremely rare ovarian tumors accounted for 1.62% (36/2210) of all cases. 36 cases of rare tumors were as follows: 1 premenarchial borderline tumor, 1 gynandroblastoma, 1 pure sertoli cell tumor, 2 sertoli-leydig cell tumor, 3 lipid (steroid) cell tumors (stromal luteoma, leydig cell tumor, steroid cell tumor NOS), 5 sclerosing stromal tumor, 3 malignant struma ovarii, 1 non-gestational choriocarcinoma, 2 primary ovarian leiomyoma, 3 leiomyosarcoma, 1 adenomyoma, 1 lipoma, 2 lipoleiomyoma, 1 hemangioma, 1 angiosarcoma, 1 paraganglioma, 1 small cell carcinoma, 2 ovarian carcinoid, 1 malignant brenner tumor, and 3 ovarian carcinosarcoma in the literature have been primarily limited to case series.

Conclusion: It is important to be aware of these rare entities in the pathological diagnosis of ovarian tumors. Intraoperative frozen examination should be performed because rare benign conditions that mimic malignancy may not require radical surgery. The rarity of these tumors makes basic scientific advances more challenging.
Poster Session I

CAN WE REDUCE FREQUENCY OF BOWEL RESECTION AND FACILITATE ABLATION OF DIAPHRAGMATIC PERITONEUM FOR THE TREATMENT OF ADVANCED OVARIAN CANCER?

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Background: Recent evidence suggest that complete resection of all disease provided a survival advantage. To improve the rate of complete cytoreduction, extensive surgical techniques such as diaphragm and bowel resection have been increasingly utilized. Although feasible, these procedures are associated with increased complexity. The aim of the study was to determine if the use of a new surgical equipment affects rates of optimal and safely surgery in case of advanced ovarian cancer.

Method: 12 patients with a FIGO stage IIIC serous ovarian cancer underwent primary surgery between january and april 2012. Clinical and pathologic data were abstracted.

Results: The median Peritoneal Cancer Index based on intraoperative assessment was 20 (15-28). In each cases a complete cytoreduction was achieved during primary surgery. Extensive surgical techniques was needed for all the patients: diaphragm resection in all the cases, splenectomy in 60% and bowel resection in 60%. For all the patients, we use PlasmaJet system, an electrically neutral energy source. It permit precise ablation of unwanted tissue with minimal damage to the adjacent and underlying structures. It allowed us to destroy the spreads of the small intestine without resection. Ablation of diaphragmatic peritoneum was facilitated (lack of muscular contractions). No majors complications were observed.

Conclusions: Complete cytoreductive surgery followed by platinum-based chemotherapy is the goal of treatment of ovarian cancer. The use of PlasmaJet in such cases is feasible. It could permit a reduction of the number of small intestine resection and seems to permit ablation of diaphragmatic peritoneum more easily. Further studies are needed.
Poster Session I

MORPHOLOGIC FEATURES ASSOCIATED WITH OVARIAN HIGH GRADE SEROUS CARCINOMAS WITH BRCA DEFICIENCIES

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1Sunnybrook Health Sciences Centre and University of Toronto, Toronto, ON, Canada, 2Memorial Sloan-Kettering Cancer Center, New York, NY, USA, 3Vancouver General Hospital and University of British Columbia, Vancouver, BC, Canada

Background and Objective: Previous study has suggested that ovarian high grade serous carcinoma (HSC) with BRCA deficiencies may be more frequently associated with solid, pseudoendometrioid and transitional (SET) features, high mitotic indexes (MI), increased tumor infiltrating lymphocytes (TILs), and geographic necrosis. This study aimed to validate this morphologic association using an independent case series.

Methods: A consecutive series of 88 HSC cases from the Vancouver General Hospital with characterized BRCA1/2 status and available histologic slides were assessed for tumor architecture (>25% SET), MI (> mean), TILs (> mean), and geographic necrosis. Histologic assessment was performed without the knowledge of BRCA status.

Results: More tumors with BRCA1 deficiency (germline or somatic mutations, or methylation) showed increased MI, TILs, or >25% SET compared to BRCA2 deficiency and BRCA unaffected tumors (Table 1). Significantly higher number of BRCA1 deficiency tumors demonstrated a combination of >25% SET with either increased MI or increased TILs (p = 0.04). No significant difference in the presence of necrosis was seen among the groups.

<table>
<thead>
<tr>
<th></th>
<th>Increased MI</th>
<th>Increased TILs</th>
<th>&gt;25% SET</th>
<th>Necrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA1 (n=36)</td>
<td>22(61%)</td>
<td>18(50%)</td>
<td>20(56%)</td>
<td>22(61%)</td>
</tr>
<tr>
<td>BRCA2 (n=5)</td>
<td>2(40%)</td>
<td>1(20%)</td>
<td>2(40%)</td>
<td>3(60%)</td>
</tr>
<tr>
<td>BRCA unaffected (n=47)</td>
<td>22(47%)</td>
<td>19(40%)</td>
<td>18(38%)</td>
<td>27(57%)</td>
</tr>
</tbody>
</table>

[Morphologic Features Associated with BRCA Status]

Conclusions: We have confirmed that tumors with BRCA 1 deficiency tend to have increased SET features in combination with increased mitosis or TILs. No morphologic trend was identified to be associated with BRCA 2 deficiency, although the case number was small.
Poster Session I

RECURRENT MALIGNANT BRENNER TUMOR OF THE OVARY COULD BE SALVAGED BY CHEMOTHERAPY: 10 CASES ANALYSIS IN A SINGLE INSTITUTE


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Ovarian Brenner tumors are rare epithelial tumors that account for 1-2% of all ovarian neoplasms. Mostly, these lesions are benign and only about 1% of Brenner tumors are malignant. We report on 10 cases with malignant Brenner tumor of the ovary including three recurrent cases with favorable prognosis after chemotherapy. Out of 78 patients with Brenner tumor of the ovary who were treated at Asan Medical Center over a 10-year period from May 1991 to January 2012, 10 cases were retrospectively reviewed from electronic medical records. The median age of the study population was 56 years. Tumor marker showed no significant association with either tumor burden or stage. The mean follow-up was 28.0 months (range 1-87 months). Recurrence was detected in 3 patients. The median recurrence time was 22 months (range 5-36 months). Three recurrent cases show favorable results. One case of stage IV showed currently no evidence of disease during 15 months after last chemotherapy. Another case of stage IIIC showed 39 months of survival after last chemotherapy. One patient of the other case of stage IIIC is currently alive with disease during 65 months after recurrence and have been managed with chemotherapy. (Table 1)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age (yrs)</th>
<th>Symptom/Sign</th>
<th>Site</th>
<th>Coexistent pathology</th>
<th>Tumor size (cm)</th>
<th>CA125 (mg/mL)</th>
<th>CA19-9 (mg/mL)</th>
<th>Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 1994</td>
<td>37</td>
<td>Abdominal pain, Vaginal bleeding</td>
<td>Unilateral</td>
<td>-</td>
<td>8.0</td>
<td>15.5</td>
<td>5.6</td>
<td>TAH c RSO</td>
</tr>
<tr>
<td>2 1999</td>
<td>42</td>
<td>Vaginal Bleeding</td>
<td>Unilateral</td>
<td>-</td>
<td>3.0</td>
<td>21.1</td>
<td>423.8</td>
<td>TAH c RSO c LS c PIND c TD c apppe</td>
</tr>
<tr>
<td>3 1999</td>
<td>59</td>
<td>Abdominal distension, Ascites</td>
<td>Unilateral</td>
<td>-</td>
<td>3.0</td>
<td>21.1</td>
<td>423.8</td>
<td>TAH c RSO c LS c PIND c TD c apppe</td>
</tr>
<tr>
<td>4 1999</td>
<td>52</td>
<td>Abdominal pain, Ascites</td>
<td>Unilateral</td>
<td>Transitional cell carcinoma (pelvic mass)</td>
<td>10.5</td>
<td>8.3</td>
<td>-</td>
<td>RSO c PIND</td>
</tr>
<tr>
<td>5 2002</td>
<td>61</td>
<td>Abdominal distension, Ascites</td>
<td>Unilateral</td>
<td>-</td>
<td>10.5</td>
<td>8.3</td>
<td>-</td>
<td>RSO c PIND c PALS c TD c apppe</td>
</tr>
<tr>
<td>6 2004</td>
<td>43</td>
<td>Abdominal distension, Ascites</td>
<td>Bilateral</td>
<td>Adenocarcinoma (bilateral ovaries)</td>
<td>10.5</td>
<td>8.3</td>
<td>-</td>
<td>RSO c PIND c PALS c TD c apppe</td>
</tr>
<tr>
<td>7 2005</td>
<td>59</td>
<td>Abdominal distension, Mass</td>
<td>Unilateral</td>
<td>Mucinous adenoma (Right ovary)</td>
<td>25.5</td>
<td>-</td>
<td>-</td>
<td>TAH c RSO c PIND c PALS c PO c apppe</td>
</tr>
<tr>
<td>8 2009</td>
<td>66</td>
<td>Abdominal Mass</td>
<td>Unilateral</td>
<td>Benign, borderline Brenner tumor (Right ovary)</td>
<td>12.5</td>
<td>-</td>
<td>138.3</td>
<td>RO *</td>
</tr>
<tr>
<td>9 2010</td>
<td>48</td>
<td>Asymptomatic</td>
<td>Unilateral</td>
<td>-</td>
<td>1.5</td>
<td>4.0</td>
<td>5.5</td>
<td>TAH c RSO</td>
</tr>
<tr>
<td>10 2012</td>
<td>61</td>
<td>Mass</td>
<td>Unilateral</td>
<td>Benign Brenner tumor (Right ovary)</td>
<td>12.0</td>
<td>10.7</td>
<td>-</td>
<td>TAH c RSO PLNS TO apppe</td>
</tr>
</tbody>
</table>

US: ultrasound; CT: computed tomography; PET: positron-emission tomography; PIND: pelvic lymph node dissection; PALS: paraaortic lymph node sampling; TO: total omentectomy; PO: partial omentectomy; apppe: appendectomy
* Malignant pathology was confirmed after removal of right ovary suspected as a benign ovarian tumor.
* Malignant Brenner tumor was found incidentally during imaging follow-up of kistoskin tumors.

[Table 1. Clinical features and disease course]
The role of adjuvant chemotherapy in malignant Brenner tumor is unclear because of its rarity. But our data showed the systemic chemotherapy have some therapeutic role in these patients even in the recurrent setting.

**Table 1. (continued)**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Metastasis</th>
<th>Chemotherapy</th>
<th>Follow up duration (months)</th>
<th>Time to recurrence (months)</th>
<th>Recurrence site</th>
<th>Current status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>IA</td>
<td>-</td>
<td>11</td>
<td>-</td>
<td>-</td>
<td>FUL</td>
</tr>
<tr>
<td>2</td>
<td>IA</td>
<td>-</td>
<td>38</td>
<td>-</td>
<td>-</td>
<td>NED</td>
</tr>
<tr>
<td>3</td>
<td>IV</td>
<td>Left SCLN</td>
<td>TC-11, HDPE, CDCA</td>
<td>34</td>
<td>5</td>
<td>Peritoneal cavity</td>
</tr>
<tr>
<td>4</td>
<td>IBC</td>
<td>Peritoneal seeding</td>
<td>TC-9, MC-1, CC-2, GTCA</td>
<td>75</td>
<td>36</td>
<td>Liver, Bladder, bone</td>
</tr>
<tr>
<td>5</td>
<td>I</td>
<td>-</td>
<td>TC#6</td>
<td>12</td>
<td>-</td>
<td>NED</td>
</tr>
<tr>
<td>6</td>
<td>IBC</td>
<td>-</td>
<td>TC#6, C#6, G#3, X#5, Bev#11, VP#6, A#2</td>
<td>87</td>
<td>22</td>
<td>Left SCLN, AMD</td>
</tr>
<tr>
<td>7</td>
<td>IA</td>
<td>-</td>
<td>83</td>
<td>-</td>
<td>-</td>
<td>NED</td>
</tr>
<tr>
<td>8</td>
<td>IA</td>
<td>-</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>FUL</td>
</tr>
<tr>
<td>9</td>
<td>IBC</td>
<td>Peritoneal seeding</td>
<td>RdC#3</td>
<td>15</td>
<td>-</td>
<td>NED</td>
</tr>
<tr>
<td>10</td>
<td>IA</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>AMD</td>
</tr>
</tbody>
</table>


* After neoadjuvant chemotherapy of TC#5, operation was done.
Poster Session I

EVALUATION OF CLINICOPATHOLOGIC ASPECTS AND TREATMENT RESULTS IN SEX CORD-STROMAL OVARIAN MALIGNANT TUMORS


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Background and aim: Ovarian sex cord-stromal tumors account for 5-8% of all ovarian malignancies. Since few studies have been conducted because of their low prevalence worldwide, our aim was to assess several clinicopathologic aspects and treatment results of these tumors.

Methods: Recorded data of 31 ovarian sex cord-stromal tumor patients referred to Ghaem and Omid university hospital of Mashhad during 1998 to 2008 were collected and analyzed.

Results: Ovarian sex cord-stromal tumors accounted for 5.9% of all ovarian malignancies. The most common pathologic form was adult granulosa cell tumor (80.6%). At the time of diagnosis, most of the patients (87.1%) were in the early stages (stage I). Overall survival rates were 95% at 2- and 5 years. Disease-free survival rates were 92% at 2 years and 79% at 5 years. Longer survival was correlated with early stages of the disease (P=0.002). Age, conservative surgery and chemotherapy had no correlation with survival (P=0.7, P=0.14, P=0.3).

Conclusion: Most of the patients with ovarian sex cord-stromal tumors are diagnosed in the early stages of the disease and in perimenopausal ages. The only factor that had a full effect on survival was the stage of the disease.
Poster Session I

SOLUBLE MUC1 AS A BIOMARKER FOR OVARIAN CANCER

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Objective: MUC1 is a transmembrane mucin and its expression is known to increase in lung, breast, ovary and colon carcinomas. MUC1 is considered as an attractive target for the immune system to attack the cancer, and currently more than 30 clinical trials targeting MUC1 are ongoing. The aim of this study is to evaluate the soluble MUC1 as a biomarker for epithelial ovarian cancer.

Methods: We collected the serum and the tumor specimens from 110 patients who were diagnosed as pelvic masses with approval of the ethical committee in our institution. We investigated the soluble MUC1 as measuring the circulating KL-6 in the serum by electrochemiluminescence immunoassay, and the MUC1 expression by IHC staining.

Results: The soluble MUC1 in epithelial ovarian cancer patients was higher than that of the patients with borderline, benign and metastatic ovarian tumors. High soluble MUC1 is observed in advanced stage tumors. We analyzed whether the soluble MUC1 would be a diagnostic marker for epithelial ovarian cancer in the patients with pelvic masses. We calculated the area under the ROC curve (AUC) of the soluble MUC1, and compared with that of CA125. The AUC of the soluble MUC1 was 0.81, which was equal to that of CA125, but with higher specificity. We also investigated the relationship between soluble MUC1 and its expression on tumors. High soluble MUC1 was observed in tumors with high MUC1 expression.

Conclusion: Soluble MUC1 is a potential diagnostic marker, and a theranostic marker for the MUC1 targeted therapy of ovarian cancer.
THE IMPACT OF SURGICAL SITE INFECTION ON VENTRAL HERNIA AFTER OVARIAN CANCER SURGERY

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Objectives: To evaluate surgical site infection (SSI) as a risk factor for the development of ventral hernia after ovarian cancer surgery.

Methods: Charts of patients undergoing primary laparotomy for ovarian cancer at the University of Wisconsin Hospitals and Clinics from 2001-2007 were reviewed. SSI was defined as infection occurring up to 30 days after surgery. Physical exam or abdominal CT scan was used to detect hernias at 1 year and 2 year end points. Other potential risk factors for ventral hernia, such as comorbidities and surgical technique, were collected.

Results: Data from 259 patients was included at 1 year, while 203 patients were followed through 2 years. The ventral hernia rate at 1 year was 9% and at 2 years was 14%. Univariate analysis showed that SSI had an odds ratio of 2.8 for the development of ventral hernia at 1 year (p=0.046), although multivariate analysis showed that only BMI and suboptimal debulking were statistically associated with ventral hernia (p< 0.001, and p=0.03 respectively). Data analysis at 2 years also showed that BMI alone was significantly associated with development of ventral hernia (p< 0.001).

Conclusions: In ovarian cancer, SSI does not increase the risk of ventral hernia. One year after surgery, both BMI and suboptimal debulking are associated with ventral hernia development while at 2 years only BMI is associated with development of ventral hernia.
Poster Session I

MICRORNA-21 OVEREXPRESSION THROUGH THE 17Q21-24 AMPLIFICATION REGULATES PTEN TUMOR SUPPRESSOR GENE EXPRESSION IN OVARIAN CLEAR CELL CARCINOMA

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Purpose: Amplification of chromosome 17q21-24 was frequently observed in ovarian clear cell carcinoma (CCC). However, the driver gene of the region is not identified. Aberrant expression of microRNAs has been shown to be involved in oncogenesis. MicroRNA-21 (miR-21) located on 17q21-24, is one of the most frequently overexpressed microRNA in many types of cancer. Based on the above, we hypothesize that miR-21 might play important roles in CCC oncogenesis through the regulation of PTEN expression.

Design: We determined 17q21-q24 copy number aberration in 28 primary CCC by comparative genomic hybridization. We measured miR-21 and PTEN mRNA expression by real-time RT-PCR analysis. Furthermore, PTEN protein expression was analyzed by immunohistochemistry. We compared miR-21 expression with the 17q21-24 copy number status and the correlation between the expression date and clinicopathological parameters including prognosis was examined.

Results: Of 28 CCC, 6 (21%) gained 17q21-24, 16 (57%) overexpressed miR-21, and 12 (43%) lost PTEN immunoreactivity. Four of 6 tumors (67%) with 17q21-24 amplification showed miR-21 overexpression. Loss of PTEN protein was found in 6 of 16 tumors (21%) with miR-21 overexpression. However, there was no significant correlation between miR-21 and PTEN expression. In total, among 6 tumors with 17q21-24 amplification, miR-21 overexpression with repressed PTEN expression was detected in two cases (33%).

Conclusion: MiR-21 is a possible target for 17q21-24 amplification in CCC.
Poster Session I

MTORC2 IS A PROMISING THERAPEUTIC TARGET IN EPITHELIAL OVARIAN CANCER

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Purpose: The mammalian target of rapamycin (mTOR) is frequently activated in epithelial ovarian cancer, and is regarded as an attractive therapeutic target for therapy. Preclinical investigations using rapamycin and its analogs have demonstrated significant growth-inhibitory effects on the growth of ovarian cancer, but those researches were focused only on mTOR Complex 1 (mTORC1), not on mTOR Complex 2 (mTORC2). We investigated the activity of mTORC2 and its role in epithelial ovarian cancer.

Experimental design: Using human ovarian cancer samples and cell lines (serous adenocarcinoma and clear cell carcinoma), we first examined the expression and activity of mTORC2. We next investigated the role of mTORC2 on the proliferation and invasiveness of ovarian cancer cells by knocking down the expression of rictor. Moreover, using 2 pairs of everolimus-sensitive parental and everolimus-resistant sublines, we examined whether mTORC2 is involved in the mechanism of acquired resistance to everolimus.

Results: mTORC2 is frequently activated in human ovarian cancer, especially in clear cell carcinoma of the ovary. mTORC2 stimulated the proliferation and invasiveness of ovarian cancer cells in vitro. mTORC2 was hyperactivated in everolimus-resistant sublines compared to their parental cell lines. Inhibition of mTORC2 activity by siRNA sensitized the everolimus-resistant ovarian cancer cells to everolimus.

Conclusion: mTORC2 is frequently activated in epithelial ovarian cancer, and is a promising therapeutic target.
Poster Session I

A CLINICOPATHOLOGIC ANALYSIS AFFECTING THE RECURRENCE AND PROGNOSIS OF 228 CASES OF OVARIAN BORDERLINE TUMOR

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Objective: To study the clinical and pathologic features and management of borderline ovarian tumor (BOT) for the aim of evaluating the risk factors that might affect the recurrence and prognosis of BOT.

Methods: 228 cases of BOT were retrospectively analyzed. Univariate and multivariate logistic regression models were constructed to evaluate the risk factors for odds ratio (OR) and statistical significance. The survival was assessed by the Kaplan-Meier method and proportional hazards model.

Results: The mean age was 36.8 years old. 141 cases were younger than 40 years old and 87 cases were equal to or older than 40 years old. FIGO stage: I, 194 cases (85.1%); II, 9 cases (3.9%); III, 24 cases (10.6%); IV, 1 case (0.4%). Histological type: serous, 137 cases (60.1%); mucous, 67 cases (29.4%); others: 24 cases (10.5%). The mean time for follow-up was 34.6 months. Recurrence was observed in 32 cases and the median time to recurrence was 31.7 months. Of these cases, 30 cases were still BOT, 2 cases had progressed to invasive carcinoma, and 1 case was pseudomyxoma peritonei. Tumor-related death occurred in 1 case. The results of the multivariate logistic regression analysis showed that conservative surgical procedures, advanced FIGO stage, infiltrating implants may be independent predictive factors of recurrence. The proportional hazards model identified that surgical procedure, FIGO stage, micropapillary growth and infiltrating implants were independently related to disease-free survival.

Conclusions: Conservative surgery is indicated when fertility is desired by young patients. Adjuvant chemotherapy after surgery cannot prevent the recurrence of BOT.
Poster Session I

EXPRESSION OF RNA BINDING PROTEINS IN OVARIAN CANCER

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Background and aims: Vertebrate RNA-binding protein family, which regulate mRNA transport, translation, turnover and some with microRNAs process is associated with cancer cells behavior i.e. migration, metastasis, apoptosis. In this study, we try to elucidate the relationship of RNA-binding proteins IMP1, IMP2, IMP3, LIN28, LIN28B and ovarian cancer.

Materials and methods: From 2002 January to 2008 January, 229 epithelial ovarian cancer cases as well as 30 normal ovarian samples were collected and analyzed. The frozen tumor tissues have been collected from patients immediately after surgical removal. Total RNA was extracted and Real-time PCR was carried out. The phospholipase-2(PLA2) used as a standard control gene. Clinical information of patients were collected and analyzed, compared with various gene expression levels.

Results: Cancer tissues with tumor cell less than 50 % or necrosis by H and E stain exam were excluded from the study. Finally, 140 ovarian cancer cases were analyzed. Data values were showed as a ratio of target gene /PLA2. In IMP family, IMP2, IMP3 are significantly up-regulated in cancer compared with normal ovaries (p < 0.05, t test). For LIN28 family analysis, patients with stage IV disease were associated with higher expression of LIN28B compared with stage I to III diseases (p < 0.05, one- way ANOVA). For survival analysis, higher expression of IMP3, LIN28B were associated with poor prognosis (log rank test, p < 0.05).

Conclusions: IMP3 and LIN28B may be candidates of prognostic biomarker in ovarian carcinoma.
Poster Session I

SCREENING AND IDENTIFICATION OF BIOMARKERS IN ASCITES RELATED TO INTRINSIC CHEMORESISTANCE OF SEROUS EPITHELIAL OVARIAN CANCERS

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Objective: Prediction of the response to chemotherapy in serous epithelial ovarian cancer (EOC) is important since intrinsically chemoresistant EOC patients (persistent or recurrent disease within 6 months) will gain little benefit from standard chemotherapy. The aim of this study was to screen and identify distinctive biomarkers in ascites of serous EOC associated with intrinsic chemoresistance by mass spectrometry.

Methods: Protein samples from ascites of 12 chemosensitive and 7 intrinsically chemoresistant serous EOC patients were analyzed using two-dimensional fluorescence difference in gel electrophoresis (2-D DIGE) coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF/TOF MS). Furthermore, the identified proteins were validated by ELISA in ascites samples from 19 chemosensitive and 9 intrinsically chemoresistant EOC patients.

Results: A total of 1523 to 1711 spots were detected in four gels by DeCyder software analysis. Thirty-four spots were differentially expressed based on the criteria of an average ratio of more than 1.5 and a student t-test P value< 0.05. After MALDI-TOF/TOF MS analysis, 11 differentially expressed proteins, including 3 up-regulated and 8 down-regulated proteins, in ascites of chemoresistant tumors were successfully identified. Of the four selected proteins (ceruloplasmin, apoliprotein A-IV, transthyretin and haptoglobin) in ascites tested by ELISA, ceruloplasmin was the only one present at significantly different levels between the chemoresistant and chemosensitive ascites samples with average concentrations of 192.2µg/ml and 157.5µg/ml, respectively (P=0.001).

Conclusion: The significantly up-regulated level of ceruloplasmin in the ascites fluid of intrinsic chemoresistant serous EOC patients suggests that it is a potential prognostic biomarker correlating with responses to chemotherapy.
Poster Session I

PREOPERATIVE EVALUATION OF SUBDIAPHRAGMATIC CARCINOMATOSIS IN EPITHELIAL OVARIAN CANCER: COMPARISON OF CONTRAST-ENHANCED FDG PET/CT AND CT

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Background and aims: Complete tumor debulking in surgery is the most important prognostic factor in advanced epithelial ovarian cancer (EOC). Preoperative imaging can help to identify patients who need radical surgery and should be referred to tertiary centres. Since surgical removal of carcinomatosis beneath the diaphragm demands expertise in upper abdominal procedures, we chose it as an indicator for need of extensive surgery. We evaluated prospectively whether subdiaphragmatic carcinomatosis can be detected preoperatively with positron emission tomography/computed tomography (PET/CT) and conventional CT.

Methods: 36 patients with suspicion of advanced EOC were scanned with a whole-body contrast-enhanced 18F-fluorodeoxyglucose (FDG) PET/CT within 2 weeks prior to laparoscopy/ laparotomy. A low-dose PET/CT was followed with a whole-body diagnostic high dose CT scan after intravenous injection of contrast agent. The results from hybrid PET/CT were compared with contrast-enhanced CT results analyzed separately from PET/CT scans. The findings in surgery were confirmed with histopathology of 49 subdiaphragmatic peritoneal biopsies and used as reference standard.

Results: Of 36 surgically staged FIGO stage IC-IV EOC patients, 31 had subdiaphragmatic carcinomatosis. Patient-based sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy for PET/CT were 76,7%, 100%, 100%, 41,7% and 80% and for conventional CT 45,2%, 100%, 100%,19% and 51,4%.

Conclusion: FDG PET/CT has high specificity and is more sensitive than conventional CT in detecting subdiaphragmatic carcinomatosis and can bring additional information when surgery is planned. However, since the NPV remains low, the readiness for radical surgery is needed also for patients with PET-negative diaphragm.
Poster Session I

IMMUNOHISTOCHEMICAL ANALYSIS OF CASES WITH CYSTIC MESOTHELIOMA OF THE PERITONEUM RESEMBLING OVARIAN TUMORS

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Aim: The aim of our study was to clarify the clinicopathological and immunohistochemical characteristics of peritoneal mesotheliomas presenting as ovarian tumors.

Method: A retrospective study of cases with benign cystic mesothelioma of the peritoneum was performed during the period 1997-2011. The clinical data of each patient were correlated with the pathological and immunohistochemical features.

Results: Three cases of benign (in patients 32-34 years old) and one case of malignant peritoneal cystic mesothelioma (aged 47 years old), respectively, are presented. Abdominal discomfort, and adnexal neoplasm was common in all patients. The cystic mesotheliomas developed in the Douglas space as multiple small cysts or large multilocular cystic mass. The malignant mesothelioma presented an extensive omental infiltration as well as of the uterus and the adnexa. The immunostains were negative to mucin, factor VIII, CA125, vimentin, CEA or secretory component, and positive to keratin in the benign tumors, while immunostains for cytokeratines were highly positive in all cells of malignant tumor.

Conclusion: Immunohistochemical analysis could be used in the correct diagnostic and therapeutic approach of such tumors.
Poster Session I

OVARIAN GRANULOSA CELL TUMORS: FROM THE CLINICAL FINDINGS TO THE PATHOLOGICAL AND IMMUNOHISTOCHEMICAL DIAGNOSIS

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Aim: Granulosa cell tumors (GCTs) represent less than 2% of all ovarian tumors. The potential of malignancy makes them clinically significant. The aim of our study was to present the clinicopathologic and immunohistochemical features of ovarian granulosa cell tumors.

Method: This is a retrospective study including all the cases of GCTs diagnosed in our laboratory over the last 10-year period. Immunohistochemical analysis for inhibin, vimentin, cytokeratin, Ki-67 and p53 was performed on archival paraffin blocks. The clinical data of the patients were correlated with the pathologic and immunohistochemical findings.

Results: Twenty-one cases (15 of the adult and 6 of the juvenile type) were retrieved. All patients were FIGO Stage I at the time of diagnosis. Recurrent disease was detected in four patients (19%) during a median follow-up of 36 months (range 2-26 years). Pathology revealed a concomitant theca-cell component in three cases, a Sertoli-Leydig component in one case, and a thecoma in one case. Archival tissue material was available in 12 cases. Immunohistochemical analysis was positive for: beta-inhibin in 12/12 cases (100%), vimentin in 11/12 cases (91.7%), cytokeratin in 3/12 cases (25%), CD34 in 0 cases (0%), and p53 in 2/12 cases (16.7%). The Ki-67 index was < 5% in 12/12 cases (100%). No significant correlations were observed between the pathologic and immunohistochemical parameters examined and the clinical outcome.

Conclusion: Despite the favorable prognosis of most GCTs, late recurrences are relatively common events even in Stage I patients, necessitating a close and long-term follow-up. The identification of novel prognostic markers, in addition to our traditional staging parameters is necessary to achieve more accurate prediction of recurrence in these patients.
Poster Session I

CLINICOPATHOLOGICAL STUDY OF EXTRAGENITAL CYSTIC LESIONS OF THE RETROPERITONEUM, THE MESENTERY AND THE PERITONEUM

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Aim: Peritoneal, mesenteric and retroperitoneal extragenital cystic lesions are rare female tumors. The aim of our study is the clinicopathological and immunohistochemical analysis of such entities.

Method: This is a retrospective study including the period 1997-2011. The pathological features are presented. Relative immunostains were also performed. Clinical data was obtained from the archives of the 2nd Department of Obstetrics and Gynecology of our Hospital.

Results: During the study period 19 cases of cystic lesions that developed in the peritoneum, mesentery, and retroperitoneum were identified. Among them 9 cases located at the retroperitoneum, 6 cases at the mesentery and 4 cases at the peritoneum. The median age of the patients was 42.3 years and the main symptom was abdominal pain. All patients underwent surgical exploration and excision of the cystic lesions. The diameter of the cysts ranged 4-27 cm and were classified as: epithelial (7/19), mesothelial (5/19), vascular (2/19), parasitic (1/19) and developmental in origin (4/19). Eighteen out of 19 cases were benign lesions and only one case was a borderline mucinous cystic tumor. Immunohistochemical analysis was performed by a streptavidin-biotin method in order to investigate CEA transcripts (MoAb, Novosan), CA125 (MoAb, CIS Diagnostics), vimentin (MoAb Ve6, Novocastra), secretory component (a polyclonal antibody, DAKO), Factor VIII (MoAb, DAKO), CD34 (MoAb, Scytec), calretinin (a polyclonal antibody, Zymed, San Francisco, CA). Cytokeratins were of low and high molecular weight (Immunon, AE1-MoAb).

Conclusion: The immunopathological characteristics of each tumor could clarify their origin and features in order to permit a correct classification of such cystic lesions which are usually benign. The treatment of choice is complete surgical excision of the tumors.
Poster Session I

CLASSIFICATION OF EPITHELIAL OVARIAN CANCER BASED ON THE STROMAL GENE EXPRESSION RELATED WITH RECURRENCE OF ENDOMETRIAL CANCER


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Aims: Cancer stroma is thought to play a role in tumor behavior including invasion or metastasis and response to therapy. We examined whether the gene expression profiles derived from cancer stroma can be used to predict the prognosis of endometrial cancers (ECs) or epithelial ovarian cancers (EOCs).

Methods: Tumor specimens were obtained from 60 ECs (I:31, II:4, III:20, IV:5; G1:19, G2:30, G3:11) and 24 EOCs (II:4, III:14, IV:6; serous:17, non-serous:7). Stromal tissues within 200 cells from tumor margins were microdissected and microarray analysis was performed. The recurrence-related genes expressed in stroma (RRGs) of ECs were selected by Cox analysis, and a gene-scoring model (GSM) was established by logistic regression. All ECs were clustered by unsupervised clustering using RRGs of ECs. All EOCs were clustered by unsupervised clustering using RRGs of ECs.

Results: Seventy-nine RRGs of ECs were selected. The AUC of ROC curve to predict the recurrence of ECs based on the GSM was 0.787. The RRG expression patterns were similar in 19 of 22 recurrent cases and in all 38 non-recurrent cases in ECs. EOCs were divided into 2 groups based on the 79 RRGs. The recurrence rates of the groups were 91% (10/11) and 54% (7/13) respectively (p=0.078).

Conclusions: This GSM can predict the prognosis of ECs. The RRG expression patterns in recurrent ECs tended to be similar with those in recurrent EOCs.
Poster Session I

AN INNOVATIVE APPROACH TO PROVIDING PATIENT EDUCATION AND SUPPORT IN OXFORD CANCER CENTRE

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Background: Oxford is the regional centre for gynaecological oncology in the Thames Valley Cancer Network. A support day for Ovarian Cancer patients from across the network was held in March 2011 - National Cancer Awareness month. The information and support day was a joint initiative between the gynaecological oncology specialist nurse team and Maggie's Oxford - a national cancer charity offering informational, psychological and emotional support to people affected by cancer.

Aims:

- To update patients on new approaches to ovarian cancer treatments
- To raise awareness of current research
- To evaluate the support needs of this patient group

Method: The day was structured around educational talks given by members of the gynaecological cancer multidisciplinary team and sessions promoting self-care and self-management by allied health professionals and family members of patients. Feedback was obtained via an evaluation form.

Results: 94 patients and their family members attended from across the network. Evaluation showed that the ability to discuss and share experiences with others was one of the most appreciated aspects of the day.

Listening to a relative's account of the experience of supporting his wife and family throughout her treatment was very powerful.

The opportunity to participate in an ovarian cancer support group was not taken up by this group on the day.

Conclusion: The opportunity to meet the gynaecology oncology multidisciplinary team in an informal setting and learn about their disease and aspects of self-management was a unique way to provide support for these patients.
Poster Session I

PK-PG ASSOCIATION ANALYSIS OF TXL IN A PHASE II TRIAL OF WEEKLY TXL/IP CBDCA THERAPY FOR OVARIAN AND PERITONEAL CANCERS

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Background and aims: Considering the enhanced efficacy of weekly administration of paclitaxel (TXL) and intraperitoneal injection of carboplatin (CBDCA), we commenced phase II clinical trial of weekly paclitaxel (TXL)/ IP CBDCA combination therapy for ovarian and peritoneal cancer patients since 2009. A high rate of adverse effects such as hematotoxicity by weekly TXL has already been reported for the JGOG3016 trial, we thus aimed to establish useful biomarkers predicting the toxicity based on genetic polymorphisms.

Methods: 47 Japanese patients of ovarian and peritoneal cancer who were eligible for the plasma TXL concentration at 0, 2, 8, and 24 hrs after the administration as of June 2011 were used for the analysis. Certain SNPs of genes including ABCB1 and CYP2C8, and deletion polymorphisms of GSTT1 and GSTM1 were determined.

Results: Patients lacks GSTM1 showed much higher levels of TXL AUC than those with wt-GSTM1 (P=0.033). Those possessing A allele at ABCB1 rs2032582 showed significantly longer MRT than others (P=0.010) and this was observed for those with wt-GSTM1 (P=0.045) but not without (P>0.3). Furthermore, combination of CYP2C8 rs11572093, CYP3A4 rs12721627 and CYP3A5 rs776746 SNPs were useful for distinguishing patients with altered levels of AUC and clearance only in the presence of GSTM1 (P=0.019 and P=0.003, respectively).

Conclusions: Stratification of patients with GSTM1 status and combinations with certain SNPs of cytochrome P450s and drug pumps were useful for identifying patients with altered pharmacokinetic parameters for TXL. These polymorphisms should be further validated in predicting adverse effects using our data set.
Poster Session I

MANAGEMENT OF ANTIANGIOGENICS' RENOVASCULAR SAFETY IN OVARIAN CANCER. SUBGROUP AND INTERMEDIATE RESULTS OF THE MARS STUDY

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¹Service ICAR, Pitie-Salpetriere Hospital, ²Medical Oncology, Tenon Hospital, ³Medical Oncology, Cochin Hospital, ⁴Medical Oncology, Pitie-Salpetriere Hospital, ⁵Medical Oncology, Curie Institut, Paris, ⁶Pharmacy, ⁷Medical Oncology, Jean Godinot Institut, Reims, ⁸Medical Oncology, Avicenne Hospital, Bobigny, ⁹Medical Oncology, ¹⁰Arterial Hypertensive, Georges Pompidou European Hospital, ¹¹Cardiology, Tenon Hospital, ¹²Nephrology, Pitie-Salpetriere Hospital, Paris, ¹³Medical Oncology, Léon Bérard Institut, Lyon, France

Background: Anti-VEGF drugs (AVD) are widely used in cancer patients (pts). Hypertension (HTN) and proteinuria (Pu) are class-side-effects of AVD, related to the inhibition of the VEGF pathway. The MARS study has been conducted to assess the renovascular tolerance (RVT) of AVD.

Methods: Multicentric prospective observational study evaluating the RVT of AVD in pts naive from any AVD, in 7 centres (2009-2011). Data collected included: gender, age, creatininemia (SCr), HTN, hematuria (Hu) and dipstick-Pu. This sub-group analysis presents the intermediate results for the first 38 pts with ovarian cancer (OC) receiving bevacizumab.

Results: Among 77 OC pts been included, 38 completed the study to date (1-year follow-up (f/u)). Median age at inclusion (AVD introduction): 62 years. Baseline assessment: HTN 7.9%, Pu 13.2%, Hu 7.9%, mean aMDRD 80.9ml/min/1.73m² and 3 pts with aMDRD< 60. Incidence of de novo Pu during f/u: 36.4% (Table). All pts with Pu at inclusion improved, except one. Among pts with de novo Pu, 58.3% afterwards improved/normalized. No Grade 3/4 Pu has been reported and no Hu. 17.1% developed HTN. Mean aMDRD decrease: -2.7ml/min/1.73m²/year. Grade 1 SCr increase: 36.4%. No thrombotic micro-angiopathy (TMA) has been reported.

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<th>Renovascular effects</th>
<th>Prevalence at inclusion (%)</th>
<th>Incidence during f/u (%)</th>
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<tr>
<td>Pu (NCI-CTC v4.03):</td>
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<tr>
<td>All Grade</td>
<td>13.2</td>
<td>36.4</td>
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<tr>
<td>Grade 1</td>
<td>10.5</td>
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<td>Grade 2</td>
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<tr>
<td>HTN</td>
<td>7.9</td>
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<td>Hu:</td>
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<tr>
<td>All</td>
<td>7.9</td>
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<td>Traces/+</td>
<td>5.3</td>
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<td>+++</td>
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<tr>
<td>SCr increase (NCI-CTC v4.03):</td>
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<tr>
<td>All Grade</td>
<td>-</td>
<td>36.4</td>
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</table>
Conclusions:

1) TMA remains rare,

2) 36.4% developed Pu, however with no Grade 3/4,

3) less than 20% developed HTN, and

4) renal function was not especially impaired.

Furthermore, in case of a renovascular effect, investigators followed the French Society of Nephrology recommendations (Halimi JM. Nephrol Ther 2008) and no treatment withdrawal for unmanageable renovascular toxicity occurred.
Poster Session I

ACTIVATION OF LIPOGENESIS BY SREBP-1 RESPONSIBLE FOR REGULATING GROWTH AND PROGRESSION OF OVARIAN CANCER

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Objective: Re-programming of lipogenic pathway is one of the most significant alterations of tumor cell physiology. Tumor cells express high levels of lipogenic enzymes most of which are transcriptional targets of sterol regulatory element-binding protein1 (SREBP-1). Our study aims to access the oncogenic potential of SREBP1 in ovarian cancer.

Methods: Immunohistochemical staining was employed to determine the expression of SREBP1 in normal ovarian tissue, benign tumor, borderline tumor, cancer and metastatic ovarian cancer samples. After conducting knockdown of SREBP1 by shRNA in ovarian cancer cell lines, cell growth, cell cycle distribution and cell apoptosis were compared among three groups including plasmid experimental group(A), negative plasmid control group(B) and no plasmid control group(C). Cell growth was measured by CCK-8 assay. Cell cycle distribution and cell apoptosis were detected by flow cytometry.

Results: SREBP1 protein expression was detected to be significantly higher in cancerous tissues than in normal control, benign tumor or borderline tumor samples (P < 0.05) by immunohistochemical staining. SREBP1 expression level was associated with the FIGO staging (P < 0.05). The cell growth was inhibited in A(P< 0.05). The cell apoptosis rate were 12.61%, 6.27%, 6.12% in A, B and C respectively. The cell apoptosis rate in A was higher than those in B or C(P< 0.05). However, no influence on cell cycle distribution was witnessed. We further studied the underlying mechanisms and found that SREBP1 is essential in cell survival.

Conclusions: The research indicates SREBP1 gene plays important roles in the tumorigenesis and development of ovarian cancer.

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Introduction: The common presentation of epithelial ovarian carcinomas includes an enlarged ovarian tumor and ascites. However, a similar presentation without definite ovarian enlargement is sometimes encountered.

Objective: The aim of this study was to evaluate the size of ovary as a predictor of prognosis for advanced stage ovarian cancer.

Methods: Among 339 patients diagnosed with advanced primary serous ovarian carcinoma from 2006 to 2011, 43 patients with normal sized ovaries (not larger than 4 cm in the longest diameter) were selected for this study after a review of the pathologic materials. Forty three patients were selected as control group with similar age, stage and baseline CA-125 level. Overall survival and disease free survival were compared between two groups during the same period.

Results: There were no difference features in age, parity, stage, grade, CA-125 level, chemotherapy between the two groups like we first designed. Median Right ovary size was 2.5cm versus 5.6cm and Left ovaries was 2.0cm versus 4.5cm. The 5-year overall survival rate was 55.7%, 87.7% for normal sized ovary group and large sized ovary group, respectively. The disease-free and overall survival in patients between two groups did not show significant difference (P=0.911 and P=0.274, respectively)

Conclusions: There was no meaningful different survival outcomes according to size of ovary(primary site) in advanced stage of ovarian cancer. Therefore, the size of ovary (primary site) could not be prognostic factor in advanced serous ovarian cancer.
Poster Session I

CHARACTERIZING THE ACTIVITY OF NATURAL PRODUCTS AGAINST OVARIAN CANCER AND DEFINING THE MOLECULAR BASIS OF RESPONSE

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Women with recurrent epithelial ovarian cancer (OVCA) receive multiple chemotherapeutics with significant toxicity. Natural, non-toxic regimens that enhance therapy and/or prolong survival are highly desirable. We evaluated three natural products; Avemar®, Quercetin, and Polyphyllin, alone and in combination with cisplatin on OVCA cells and sought to define the molecular pathways that determine response.

Methods: Ten OVCA cell lines were subject to increasing doses of Avemar®, Quercetin, and Polyphyllin, +/- cisplatin. Sensitivity was quantified by MTS cell-viability assays (IC50). Affymetrix HuRSTA microarray gene expression analysis and Pearson's Correlation test of IC50 values and expression-data was performed. Genes associated with IC50 were identified and subject to biological pathway analysis.

Results: Avemar®, Quercetin, and Polyphyllin all exhibited significant anti-proliferative effects on OVCA cells. A potentiation of cisplatin cell death occurred in 8/10 Avemar®, 2/10 Quercetin and 8/10 Polyphyllin, cell lines. Pearson's correlation of gene expression data and IC50 values identified 580, 671 and 550 genes associated with sensitivity to Avemar®, Quercetin, and Polyphyllin, respectively (p< 0.01). Genes associated with OvCa sensitivity included 50(Avemar®), 69(Quercetin), and 37(Polyphyllin) unique biological pathways (p< 0.01); and was associated with three common pathways: Cell Cycle Regulation of G1/S transition, Development/Role of Activin A in cell differentiation/proliferation, and Signal transduction/Activin A signaling regulation.

Conclusions: Avemar®, Quercetin, and Polyphyllin have significant in-vitro activity against OVCA cells and may potentiate the effect of cisplatin. Genome-wide expression data reveals the biologic pathways that underlie response. Our data and the safety/tolerability of these natural products, supports their clinical evaluation in women with OVCA.
Poster Session I

OBSTETRICIAN/GYNAECOLOGISTS ATTITUDES TO SALPINGECTOMY IN PREVENTION OF TUBO-OVARIAN CANCER: A WILLINGNESS TO CHANGE

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There is increasing histopathological and molecular evidence that the site of origin of serous cancers of the pelvis (SCP) is the fallopian tube, particularly when the SCP is high grade and arising in women with BRCA mutations. Changing general gynaecological practice to incorporate more opportunistic salpingectomy has the potential to reduce the incidence of serous pelvic cancers (SPC). We sought the opinions of Obstetrician/Gynaecologists working in Irish Hospitals by electronic survey to determine their attitudes to incorporating salpingectomy into their practice of female sterilisation, hysterectomy for benign conditions, and electively for young BRCA mutation carriers who want to postpone oophorectomy.

In their current practice 96% performed tubal sterilisation by clipping at laparoscopy and 4% performed salpingectomy. 73% were willing to consider salpingectomy. Tubal ligation at C/Section is currently performed by cutting +/-removal of part of fallopian tube (79%) and salpingectomy (12%). 82% would be willing to offer salpingectomy for sterilisation at C/Section. Concerns regarding the adoption of salpingectomy were more difficult surgery (44%) and irreversibility (36%).

Salpingectomy is performed at hysterectomy (without oophorectomy) for benign conditions by 26% at abdominal (AH) and 4.5% at vaginal hysterectomy (VH). 90% would now consider salpingectomy at AH and 66% at VH. Respondents thought salpingectomy would make surgery more difficult in AH (38%) and VH (74%).

Two thirds of correspondents would consider salpingectomy for women at genetic risk of ovarian cancer who wanted to postpone oophorectomy.

A programmes of ovarian cancer prevention that includes salpingectomy in these surgical scenarios is likely to succeed in Ireland.
ELECTIVE SALPINGECTOMY IN THE PREVENTION OF TUBO-OVARIAN CANCER: A SURVEY OF OBSTETRICIAN/GYNAECOLOGISTS’ ATTITUDES

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There is increasing histopathological and molecular evidence that the site of origin of serous cancers of the pelvis (SCP) is the fallopian tube, particularly when the SCP is high grade and arising in women with BRCA mutations. Changing general gynaecological practice to incorporate more opportunistic salpingectomy has the potential to reduce the incidence of serous pelvic cancers (SPC). We sought the opinions of Obstetrician/Gynaecologists working in Irish Hospitals by electronic survey to determine their attitudes to incorporating salpingectomy into their practice of female sterilisation, hysterectomy for benign conditions, and electively for young BRCA mutation carriers who want to postpone oophorectomy.

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A programmes of ovarian cancer prevention that includes salpingectomy in these surgical scenarios is likely to succeed in Ireland.
Poster Session I

PERITONEAL TUBERCULOSIS MIMICKING OVARIAN CANCER IN THREE PATIENTS

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Introduction: Peritoneal tuberculosis is a rare disease that mimicks ovarian malignancy and consist of 3/3% of cases of extra-pulmonary tuberculosis (TB).

Method and patients: We describe three patients with the complete physical examination, and medical and family history, routine biochemical test and level of CA-125 chest X-ray and abdominal ultrasonography record of women with symptom abdominal pain, ascitis, weight loss who referred to shahid sadoughi hospital.

Results: Three patient with pritoneal tuberculosis mimicking ovarian cancer were encountered. All of the patient had abdominal pain, elevated serum CA125 and one of them had fever and severity ascitis. Cystoscopy in on patient and laparotomy in two patients revealed peritoneal TB and no malignancy. All of the patients treated with quadruple anti -TB drugs and we follow up our patient for 6 month.

Conclusion: It is very important that a gynecologist attend to this symptom and don’t mistake and don’t lead to the performance of an unnecessary extended surgery. The diagnosis TB and ovarian carcinoma is very difficult and most do examination of ascitis fluid by para-centesis and histopathology examination of biopsy from pelvic mass taken and give correct diagnosis in this study we done 2 unnecessary surgery.
Poster Session I

EVALUATION OF CA-125 LEVEL AND ITS RELATION TO THE SIZE, TYPE OF HISTOLOGY, BENIGN OR MALIGNANCY, SURVIVAL RATE AND POSTOPERATIVE COMPLICATIONS IN PELVIC MASS

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Pelvic masses are common clinical findings and are seen in women in all age groups. About 8% of women 20 to 40 years old who had no symptoms and were randomly examined had pelvic cystic masses larger than 2.5 cm. we evaluated designed the relationship between the level of tumor marker CA125, tumor size, histopathological reports, metastases and benign or malignancy status.

Material and method: A retrospective cross-sectional descriptive study. Information, using questionnaires, was collected from patients who were visited the Shahid Sadoughi Hospital from 1386 to 1389 because of pelvic mass. Data were analyzed using software SPSS v.14 (SPSS Hnc, Chicago, USA).

Result: Overall, 92 patients (45.3%) had mass dimension less than 7 cm and 111 patients (54.7%) had a mass greater than 7 cm. In 130 patients (64%) the CA-125 levels were normal and 73 patients (36%) had increased values. Statistical analysis, based on Fisher’s Exact Test, showed that there is no significant relationship between CA-125 level and tumor size (P value = 0.883).

Masses, based on ultrasound features, were classified as: cystic, solid and heterogeneous. Statistical analysis, based on Fisher’s Exact Test, showed no significant relationship between CA-125 levels and the characteristics of ultrasound (P value = 0.297). CA-125 levels demonstrated a significant association with post operation complications (P value = 0.001).

Conclusion: Around the age of menopause only a limited number of tumor markers including the level of CA125, and, if there is an indication, CEA and CA 19-9 should be checked and there is no need to check all the tumor markers.
Poster Session I

LC-MS E DETECTS PROTEINS DIFFERENTIALLY EXPRESSED IN TISSUE AND SERUM FROM PATIENTS WITH BENIGN AND MALIGNANT OVARIAN TUMORS

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Introduction: In this study, we used a new and powerful mass spectrometry approach called LC-MS E, to identify potential protein markers and pathways playing a role in ovarian cancer development and progression.

Materials and methods: We used LC-MS E to measure and compare the protein content of serum and tissues from six patients with serous adenocarcinoma and six patients with serous cystadenoma of the ovary. We used laser microdissection to collect homogeneous regions of cells with uniform histology. Data were analyzed using moderated t-tests and Benjamini-Hochberg false discovery rates. Adjusted p-values of < 0.05 were considered significant.

Results: In the serum specimens, 13 proteins were identified with different concentrations in malignant versus benign sera. Proteins included abundant serum proteins such as apolipoprotein A1 and transferrin. In the tissue lysates, 27 proteins were differentially expressed. For a large subset of these proteins literature searches confirmed roles in ovarian cancer related to e.g. cell motility and invasion (myosin-9), chemoresistance (decorin), and survival (60 kDa heat shock protein). In both datasets, differential expression was also observed for proteins that have not previously been associated with ovarian cancer, such as C9 and Afamin (serum), and Prolargin and Ubiquitin-like modifier-activating enzyme 1 (tissue).

Conclusion: Our study revealed several protein changes in serum and tissues from patients suffering from benign and malignant ovarian tumors. Some proteins were already known to play a role in ovarian cancer, others are new candidates which may provide new insights into the etiology of the disease or act as potential new disease markers.
Poster Session I

THE EFFECTS OF ELECTROMAGNETIC FIELD (EMF) ON OOCYTE IN RAT (AN ELECTRON MICROSCOPIC STUDY)

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Background: With the increase in modern technology, many industrial and household appliances, which we take for granted to be safe expose the public to magnetic fields. Various studies using rodents as experimental models have attempted to elucidate the reproductive toxic effects of exposure to weak magnetic fields and the results have been found to be rather contradictory. During the last decade genicular systems have been extensively studied and their vital importance for normal function is generally accepted and established their role in their regulation for spermatogenesis and oogenesis.

Objective: The aim of this study was to evaluate the effects of Electromagnetic field (EMF) on in-vitro rat postnatal oocyte development.

Materials and methods: A total of 40 male and 40 female Wistar rats (about 15 week-old) procured from animal house were used for the study. Females were observed for the sign of pregnancy i.e., vaginal plugging on the next day. Of the 40 breeding female rats, 30 rats at random were selected for exposure to EMF as experimental group and 10 as control group (unexposed).

Result: It showed heterochromatism and condensation of oocyte cell nucleus. Depopulation of follicles was seen. The empty spaces between the granulose and theca cells appeared.

Conclusion: The results suggest that EMF exposure causes profound changes in the oocyte on long term exposure it could result in irreversible damage which may lead to sub fertility. It is suggested that long term exposure should be avoided.
Poster Session I

TRABECTEDIN - BASED COMBINATIONS IN TREATMENT OF PLATINUM-SENSITIVE RECURRENCE EPITHELIAL OVARIAN CANCER (EOC). PILOT STUDY

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Background: Standard treatment for pl-sensitive recurrence EOC is pl-based combinations. OVA-301 study showed greater efficiency Trabectedin+PLD in the pl-sensitive pts. Purpose of the study was comparing pl. vs non-pl. trabectedin-based regimens in this pts.

Methods: 14 pts with pl-sensitive EOV were enrolled. Median of age was 55. The mean number of prior chemotherapy lines was 2. All pts had ECOG PS 0-1. The pts were randomized: Trabectedin 1.1-0.8mg/m² + Cisplatin 75-50mg/m² (TC) 1d in 21d cycle vs Trabectedin 1.1-0.8mg/m² + Doxorubicine 30-25mg/m² (TD) 1d in 21d cycle. Initial doses were reduced due to toxicity. The primary endpoint was response (RECIST) and safety.

Results: 12 pts were evaluated. 28 cycles of treatment were conducted. The mean number of cycles was 2.3.

Arm 1 TC (n=6): 4 pts had SD, 2 pts - PR. The most frequent AEs gr.I-II were nausea 57.1%, weakness 57.1%, anemia 57.1%, thrombocytopenia 50%, neutropenia 35.7%, vomiting 14.3%, hepatotoxicity 7.1%, stomatitis 7.1%, nephrotoxicity 7.1%. AEs gr.III-IV were neutropenia 42.8%, thrombocytopenia 35.7%, weakness 35.7%, hepatotoxicity 7.1%, nausea 7.1%, vomiting 7.1%.

Arm 2 TD (n=6): 1 pts had PD, 2 - SD, 1 - PR, 1 - CR. The most frequent AEs grade I-II were nausea 85.7%, weakness 57.1%, hepatotoxicity 50%, anemia 50%, thrombocytopenia 36.3%, neutropenia 14.3%, vomiting 14.3%, nephrotoxicity 14.3%, stomatitis 14.3%. AEs gr. III-IV were neutropenia 57.1%, weakness 21.4%, hepatotoxicity 14.3%, thrombocytopenia 14.3%, vomiting 7.1%.

Conclusion: Trabectedin-based combinations shown reassure results, but the toxic profile necessitates to search the optimal dose regimens.
Poster Session I

EXPRESSION PROFILES IN OVARIAN CANCER (OC)

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Background: Tumor heterogeneous and differently respond to chemotherapy.

Methods: 85 FFPE tumors blocks and serum blood from 136 OC pts (IC-IIVst.) who received platinum-taxane therapy in 1-line were analyzed by expression of EGFR, VEGF, ER, EP, p53, ki-67, HER2, BRCA 1/2 mut. and were associated with PFS. The status of expression was measured by immunohistochemical analyses (85 pts), BRCA 1/2 mut. was measured by method ASH.

Results: Median follow-up for PFS endpoint was 41 months. Median PFS were 23.5 m. (BRCA 1/2 mut. - 17pts) and 19.3 m. (BRCA 1/2 wild - 119 pts) (p=0.072). 17 pts with BRCA 12 mut. had serous adenocarcinoma G2-G3. All 85 pts had 0% expression HER2. 96.4% of pts. had high level of VEGF (range 50-100%), 58.8%- high level of EGFR (range 30-75%), 81.2% of pts had positive ER (range 1-100%), 49.4% - positive EP (range 1-96%). 69.4% of pts had > 10% positive tumors cell expression for p53 (high expression), 64.7% of pts had > 40% positive tumors cell expression for ki-67 (high expression), 8.2% of pts had 0-20% positive tumors cell expression for ki-67 (low expression). High expression of ki-67 was significantly associated with low PFS (13.2 m. v.s 19.4 m. p=0.041). Pts with positive ER had PFS 18.3 m. v.s 16.1 m. with negative ER (p=0.064). Expression of EGFR, VEGF, EP, p53 were not correlated with PFS.

Conclusion: We found no significant association status of BRCA 12, expressions of EGFR, VEGF, EP, p53 with PFS. High expression of ki-67 was a poor prognostic factor for OC.
Poster Session I

EFFECT OF THE USE OF GRANULOCYTE COLONY-STIMULATING FACTOR ON RECURRENCE IN PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Objective: To evaluate the effect of granulocyte colony-stimulating factor (G-CSF) use on recurrence in patients with epithelial ovarian cancer.

Methods: A retrospective chart review was performed on patients with stage I-IV epithelial ovarian cancer who underwent debulking surgery and adjuvant platinum-based chemotherapy between 2000 and 2006. Patients who received neoadjuvant chemotherapy and interval cytoreduction were also included. Progression-free survival (PFS) was defined as the time interval from surgery or neoadjuvant chemotherapy, whichever occurred first, to the first evidence of recurrence. The effect of G-CSF use on PFS was estimated by Kaplan-Meier method and log-rank test. Clinicopathologic variables were also compared between G-CSF users and non-users by chi-square test and Student's t test.

Results: Two hundred forty-four patients were eligible for analysis; 114 patients (46.7%) used G-CSF and 130 patients (53.3%) did not use G-CSF during the neoadjuvant or adjuvant chemotherapy. There were no differences in age, stage, and histology between G-CSF users and non-users. However, G-CSF users tended to have residual disease after surgery more frequently (p=0.060), and received more cycles of chemotherapy (7.6 vs. 6.7 cycles; p=0.001). In overall, there was no difference in PFS (p=0.944) and recurrence rates (63.8% vs. 60.5%; p=0.593) between G-CSF users and non-users.

Conclusions: The use of G-CSF during the first-line chemotherapy did not affect the recurrence in patients with epithelial ovarian cancer.
Poster Session I

THE RATIO OF STANDARDIZED FLUORINE-18 FLUORODEOXYGLUCOSE UPTAKE ON PREOPERATIVE POSITRON EMISSION TOMOGRAPHY/COMPUTED TOMOGRAPHY: PROGNOSIS PREDICTOR IN ADVANCED EPITHELIAL OVARIAN CANCER

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In advanced epithelial ovarian cancer, to assess the prognostic value of the ratio of standardized uptake value (SUV) of fluorine-18 fluorodeoxyglucose (18F-FDG) on positron emission tomography/computed tomography (PET/CT) for predicting incomplete cytoreduction, recurrence and survival before operation.

From May 2004 to December 2009, 158 patients with advanced epithelial ovarian cancer underwent 18F-FDG-PET/CT followed by surgical staging in our institution. We measured the ratio of the SUV$^{\text{max}}$ in the upper abdomen region and the lower abdomen region (UA/LA SUV$^{\text{max}}$) where were divided at the level of umbilicus. Cox proportional hazards analysis and Kaplan-Meier method were used to identify the predictors for recurrence and survival. Using the Mann-Whitney U-test, the UA/LA SUV$^{\text{max}}$ in patients undergoing complete debulking was compared with incomplete debulking.

The median age was 54 years. The median follow-up period was 28 months. 132 were stage III, and 26 stage IV. There were 116 (73.4%) cases of recurrence and 50 (31.6%) cases of disease specific death. In multivariate analysis, high UA/LA SUV$^{\text{max}}$ and incomplete debulking were significantly associated with recurrence and high UA/LA SUV$^{\text{max}}$ and histology (clear cell and carcinosarcoma compared with serous, mucinous and endometrioid type) were significantly associated with disease specific death. SUV$^{\text{max}}$ in the primary tumor was not associated with both recurrence and disease specific death. The UA/LA SUV$^{\text{max}}$ in cases of incomplete debulking was significantly elevated compared with complete debulking.

High UA/LA SUV$^{\text{max}}$ on preoperative 18F-FDG-PET/CT is an important factor for poor prognosis and could be a predictor for incomplete debulking in advanced epithelial ovarian cancer.
Poster Session I

EXPRESSION AND SIGNIFICANCE OF TLR4/MYD88 SIGNALING PATHWAY IN OVARIAN EPITHELIAL CANCERS

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The Toll-like receptor (TLR) 4/MyD88 signaling pathway has been shown to have oncogenic effects. To demonstrate the role of TLR4/MyD88 signaling in ovarian epithelial cancers (OECs), we examined the expression of TLR4, MyD88 and NF-κB in OECs. The expression of TLR4, MyD88, and NF-κB were detected by immunohistochemistry and the relationship between these proteins and clinicopathologic features were also analyzed in 123 cases of OECs. The expression of TLR4, MyD88, and NF-κB in OECs was 46.3% (57/123), 36.6% (45/123) and 65% (80/123), respectively. Their expressions were associated with histologic type of OECs, particularly clear cell type. There was no significant correlation between TLR4 or NF-κB expression and histologic grade, tumor size, mitotic count, FIGO stage, disease recurrence. However, there was significant correlation between the expression of MyD88 and FIGO stage, disease recurrence as well as histologic type. In univariate analysis, the expression of TLR4, MyD88, and the co-expression of TLR4/MyD88, TLR4/MyD88/NF-κB had a significant impact on survival of patients with OECs. Only MyD88 expression had an independent prognostic significance in multivariate analysis. Our findings suggest that the TLR4/MyD88 signaling pathway is associated with the survival of OECs and MyD88 is an independent prognostic predictor of patients with OECs. TLR4/MyD88 signaling pathway may be a mechanism of poor prognosis in clear cell type of OECs.
Poster Session I

VALUE OF SERUM CA125 LEVELS IN RECURRENT EPITHELIAL OVARIAN CANCER WITH COMPLETE REMISSION TO PRIMARY THERAPY

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Objectives: The aim of this study was to ascertain whether serum CA125 level is the prognostic value in patients with recurrent epithelial ovarian cancer who have achieved a complete response to primary treatment.

Methods: Between January 1995 and April 2007, we reviewed the records of 134 recurrent ovarian cancer patients who reached complete remission (i.e. no physical or radiological signs of residual disease and CA125 values ≤ 35 U/mL) after primary treatment were included. A receiver operating characteristic curve was used to determine the most useful CA125 level in predicting overall survival (OS) and Cox proportional hazards models adjusted for covariates were used for analyses.

Results: The 5-year OS rate was 25.3%. The optimal cutoff point of CA125 after completing adjuvant chemotherapy to predict disease progression was 10 U/mL (sensitivity, 76.0%; specificity, 76.5%). On multivariate analysis, CA125 level > 10 U/mL after primary treatment was an independent prognostic factor predictive for disease progression. The risk of recurrence was higher for CA125 level > 10 U/mL (hazards ratio = 2.869; P < 0.001). The 5-year OS rate for patients with CA125 level ≤ 10 U/mL was 52.0%, which was higher than a OS of 9.5% for CA125 > 10 U/mL (P < 0.001).

Conclusions: CA125 level after primary treatment is a strong independent prognostic factor for recurrent epithelial ovarian cancer who has achieved a complete response to primary treatment.
GENETIC ALTERATIONS RELATED TO THE PROGNOSIS OF EPITHELIAL OVARIAN CANCER

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Objectives: This study is to investigate the prognostic factors of epithelial ovarian cancer based on the genomic alterations and to suggest the pre-clinical evidences that predict the treatment response and decide the individual targeted therapy.

Methods: We obtained DNA samples from paraffin blocks of 20 patients who showed the different prognosis after the initial treatment for epithelial ovarian cancer. After analyzing the copy number variation (CNV) related to the prognosis by array comparative genomic hybridization (aCGH), the candidate genes were validated by real-time RT-PCR.

Results: Significant CNVs according to the prognosis of epithelial ovarian cancer appeared in 125 genes. There were 74 genes that showed the gain of CNVs in patients with poor prognosis; including monoamine oxidase A (MAOA), solute carrier family 28-member 3 (SLC28A3), SHQ1 homolog (SHQ1), etc. There were 51 genes that showed the loss of CNVs in patients with poor prognosis; programmed cell death 6 interacting protein (PDCD6IP), platelet-derived growth factor receptor (PDGFR), SHC SH2-domain binding protein 1 (SHCBP1), etc. We confirmed the mRNA expression of 15 candidate genes that showed the gain of CNVs. SHC1, PACSIN, HSPB2, and YY1 were significantly overexpressed in patients with poor prognosis.

Conclusions: Genetic alterations were related to the different prognosis of epithelial ovarian cancer. In this study, the overexpression of SHC1, PACSIN, HSPB2, and YY1 was represented to the significant poor prognostic factors. Further evaluation is necessary to develop the predictive or prognostic markers for epithelial ovarian cancer.
Poster Session I

A NEW PROGNOSTIC INDEX MODEL USING META-ANALYSIS IN EARLY-STAGE EPITHELIAL OVARIAN CANCER

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Objectives: To construct a novel prognostic index (PI) model of early-stage ovarian cancer (EOC).

Methods: PI model was constructed through meta-analyses. The methodological quality of the studies was assessed using the modified Jadad scale for randomized controlled trials (RCTs) and the Newcastle-Ottawa Scale for non-RCTs. The prognosis factors of the PI model that had a significant impact on the recurrence-free survival (RFS) of patients with early-stage ovarian cancer were chosen. A total of 177 patients with early-stage ovarian cancer who were treated at Severance Hospital were analyzed using the new PI model to test its utility.

Results: The equation PI = 2 × age + 86 (if grade 2) or 105 (if grade 3) + 53 (if stage Ib or Ic) or 130 (if stage II) + 53 (if no lymphadenectomy) - 43 (for adjuvant chemotherapy of 3 times or more) + 10 (calibrating constant) was derived. Based on PI values, the high-risk group showed a significant 5-year-RFS difference compared to the low-risk group (P-value < 0.01 by log-rank test) and a borderline significance in comparison to the intermediate-risk group (P-value=0.08). When the cutoff level of PI values was set at 211, the low- and high-risk groups of recurrence within 5 years were also identified by Cox regression analysis (HR=7.25, 95% CI: 2.98-17.65).

Conclusions: Our PI model was predictive in this study and may be effective in clinical practice. Prospective studies should be conducted to confirm the predictive ability of the new PI model for early-stage EOC recurrence.
Poster Session I

UPPER ABDOMINAL SURGERY IN OVARIAN CANCER DEBULKING PROCEDURES

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Objective: Upper abdominal surgery in ovarian cancer debulking procedures is often required to achieve complete cytoreduction (no visible disease).

Methods: A retrospective study of 31 patients with primary ovarian cancer who underwent upper abdominal surgery between 1996 and 2011 at The Royal Marsden Hospital.

Results: Median age at time of upper abdominal surgery was 55 years (range, 38-76 years). All patients underwent primary or delayed primary debulking surgery; in 8 patients who underwent secondary/tertiary cytoreductive surgery the median interval between diagnosis and surgery was 3.9 years (range, 9 months-7 years). 25/31 (81%) had advanced disease (histopathological stage 3/4) at initial diagnosis. 17/31 (55%) had chemosensitive disease (10 did not receive adjuvant therapy at primary treatment). Procedures included: splenectomy (11); diaphragmatic stripping/peritonectomy (8); hemi/subtotal/ colectomy (8); liver resection (4); subtotal/distal pancreatectomy (3, 1 case benign); subtotal/total gastrectomy (2); adrenalectomy (1, benign); porta hepatis disease (1). 26/31 (84%) had residual disease ≤1cm including 20 (64.5%) patients in whom R0 resection was achieved. Median operating time was 275 mins (range, 95-500 mins) with a mean blood loss of 1.75 litres (range, 250ml-8 litres). 24/31 (77%) received blood products perioperatively. Median in-patient stay was 11 nights (range, 6-26). 22/31 (71%) received further chemotherapy postoperatively. 3/31 (9.6%) had a complication Grade III or IV (Clavian-Dindo classification); there was no operative mortality. Cox multivariate regression analysis could not identify any factors predictive of complete cytoreduction. The median survival from time of surgery was 5.4 years (range, 3.7-7 years).

Conclusion: A multidisciplinary approach in carefully selected cases is crucial in achieving the paradigm shift of complete cytoreductive surgery without increasing morbidity or mortality.
Poster Session I

ASSESSING ADNEXAL MASSES FOR MALIGNANCY: A COMPARISON OF FOUR DIAGNOSTIC MODALITIES

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The objective of this analysis is to assess the diagnostic accuracy of four different modalities in the evaluation of suspicious adnexal masses (preoperative imaging, tumor markers, video-assisted laparoscopic intraoperative assessment, and frozen section), as compared with final pathology.

One hundred thirty-one patients presenting at two urban university-affiliated community hospitals with a preoperative diagnosis of adnexal mass were included, excluding patients with preoperative signs of advanced ovarian cancer.

Patients underwent diagnosis with one or more of the following: imaging, tumor markers, videolaparoscopic management with intraoperative assessment, and/or frozen section.

Of 131 patients evaluated, 44 had tumor markers examined, 127 had imaging performed (pelvic ultrasound, CT, and MRI), and 87 had specimens evaluated with frozen section. One hundred twenty-nine patients were assessed intraoperatively by a gynecologic oncologist. There were 24 (18.3%) borderline/invasive malignancies and 107 (81.7%) benign pathologies.

The single most accurate test was intraoperative impression (96.9% accurate), followed by frozen section (95.4% accurate). Combined, intraoperative assessment and frozen section yielded 91.7% sensitivity and 99.1% specificity, with an accuracy of 97.7%.

<table>
<thead>
<tr>
<th>Method of Evaluation</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
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<tr>
<td>Frozen section</td>
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<td>98.5</td>
<td>94.7</td>
<td>96.0</td>
<td>95.4</td>
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<tr>
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<td>60.6</td>
<td>97.0</td>
<td>87.4</td>
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<td>83.9</td>
<td>64.3</td>
<td>84.0</td>
<td>77.8</td>
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<tr>
<td>Intraoperative impression</td>
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<td>100</td>
<td>100</td>
<td>96.0</td>
<td>96.9</td>
</tr>
<tr>
<td>Frozen section + Intraoperative impression</td>
<td>91.7</td>
<td>99.1</td>
<td>95.7</td>
<td>98.0</td>
<td>97.7</td>
</tr>
</tbody>
</table>

Frozen section combined with intraoperative impression is the most accurate method of differentiating between malignant and benign adnexal masses at laparoscopy.
Poster Session I

DUAL INHIBITION OF PI3K AND MTOR USING NVP-BEZ235 AS A NOVEL APPROACH TO TREAT MUCINOUS ADENOCARCINOMA OF THE OVARY

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Objective: Mucinous adenocarcinoma of the ovary (MAC) has a poor prognosis, in part because it resists standard chemotherapy. Activating the phosphatidylinositol-3'-kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR) pathway seems to indicate drug resistance and poor prognosis in ovarian cancer and, therefore, may be an attractive target for therapy. The present study assessed the possibility of molecular targeted therapy to treat MAC with NVP-BEZ235 (BEZ235), a dual inhibitor of the PI3K and mTOR.

Method: The sensitivity of four cell lines of MAC (TU-OM-1, RMUG-S, RMUG-L, and OMC-1) to BEZ235 was determined with the WST-8 assay. Cell cycle distribution was assessed by flow cytometry, and the expression of proteins in apoptotic pathways and molecules downstream of the PI3K/Akt/mTOR signaling pathways were determined by western blot analysis.

Results: The half-maximal inhibitory concentration values of each cell line ranged from 18 to 118 nM for BEZ235. The protein expression levels of phosphorylated (p) Akt, pp70S6K and p4E-BP1 were suppressed after exposure to BEZ235 in a dose-dependent manner. After treatment with BEZ235, the proportion of the cells in the G0/G1 phase increased, and the proportion of the cells in the S phase fraction decreased. Moreover, 24 h after being treated with BEZ235 the protein expression of cleaved PARP and caspase-9 increased in both TU-OM-1 and RMUG-S cells.

Conclusion: The PI3K/Akt/mTOR pathway is a potential therapeutic target for MAC and indicate that BEZ235 is worth exploring as a therapeutic agent for MAC.
Poster Session I

IS THERE A PLACE FOR NEOADJUVANT CHEMOTHERAPY IN THE TREATMENT OF ADVANCED MALIGNANT GERM CELL TUMORS OF OVARY?

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Background: There is limited data on the role of neoadjuvant chemotherapy (NACT) in advanced malignant germ cell tumors of ovary (MOGCT).

Methods: 23 patients (median age 19 years, range, 14 to 35) with FIGO stage III-IV and ECOG performance status 3-4, received 4 cycles of NACT followed by fertility sparing surgery. Pre-treatment all patients underwent biopsy, tumor markers and imaging studies. Histopathology - dysgerminoma-14, mixed GCT - 6 and endodermal sinus tumor-3.

Results: 21/23 patients responded to NACT; CR-16, PR-5. 18 of 21 responders underwent U/L salpingo-oophorectomy, omentectomy and lymph node sampling. 13/18 patients had pathological CR; five had residual disease and achieved CR following 2 more cycles of BEP. Three patients refused for surgery; 2 relapsed at 9 and 12 months and achieved CR following salvage chemotherapy and surgery, third patient continues to be alive and disease-free. Estimated overall survival at 10 years is 95.2% (95% CI 199.5 to 239.6). 17/21 patients have resumed menstruation, 9/17 are married, 8/9 have conceived and delivered 12 healthy children. We compared their outcome with 61 patients of advance disease treated with primary surgery followed by 4 cycles of BEP. Age (p=0.5), stage (p=0.37), pathology subtype (p=0.07) were not different. Mean survival in NACT and advanced disease group is 105.9 (95% CI 80.1-131.8) and 104.6 (95% CI 86.4-122.1), p=0.50, respectively.

Conclusion: Neoadjuvant chemotherapy using BEP is a reasonable approach for patients with advanced MOGCT who are not suitable candidates for surgery.
Poster Session I

BEVACIZUMAB IN PATIENTS WITH HEAVILY PRETREATED OVARIAN AND OTHER MULLERIAN CANCERS: A SINGLE-INSTITUTION EXPERIENCE

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Background: Bevacizumab (Bev) is as active as any salvage chemotherapy (CTx) in patients (pts) with recurrent ovarian (OC) and other Mullerian carcinomas (MTC). We hereby report on our single-institution experiences with Bev based systemic therapy (Tx) in pts with heavily pretreated MTCs.

Methods: A total of 72 intensively pretreated MTC pts (ovarian: n=63; fallopian tube: n=2; type II endometrial: n=4; peritoneal: n=3) who did not qualify to be recruited onto a clinical trial have been included in this analysis. Pts had received a median of 4 (range 2-4) prior CTx. 42 were Platinum-resistant. Bev (10 mg/kg q2w or 15 mg/kg q3w) was given as single agent (group A, n=12), alongside with metronomic Ctx (group B, n=40), or combined with conventional Ctx (group C, n=20).

Results: Most common Bev related side effects were hypertension, proteinuria, headache, infection, epistaxis and subileus which were not Tx limiting except 2 pts. Median TTP was 25.7 wks and median OS was 55.1 wks with no difference between Pt-resistant and Pt-sensitive pts. In regard to TTP, there was a non-significant trend favoring group B (36.4 wks) vs group A or B (22.9 and 19.2 wks). Regarding OS, group A (63.0 wks) or B pts (70.4 wks) did significantly better than group C pts (35.4 wks, p=0.03).

Conclusion: Bev-based Tx was active and well tolerated in pts with heavily pretreated MTC. Clinical Pt-resistance did not predict a worse clinical outcome. However, Bev should be preferably given as single agent or combined with metronomic Ctx.
Poster Session I

THE SIGNIFICANCE OF COMBINATION CHEMOTHERAPY IN OVARIAN CANCER AT A POPULATION LEVEL

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Background: Controversies in the management of epithelial ovarian cancer have resulted in differences in practice. The objective of this study was to evaluate different strategies for administering first-line chemotherapy in ovarian cancer and to determine their effect on survival at a population level.

Methods: This was a retrospective population-based study of 854 women diagnosed with epithelial ovarian cancer in British Columbia, Canada, from 2005-2008. The BC Cancer Registry provided data on stage, grade, histotype, date of surgery, surgeon type, first-line chemotherapy including type and number of cycles, cause of death, and date of death. Chart review on all Stage IIIC and IV patients was undertaken to evaluate extent of surgical debulking. A Cox regression model evaluated the association of covariates on overall survival.

Results: Of 820 women eligible for chemotherapy, 714 received treatment (87.1%), including 103 (12.5%) who received single-agent carboplatin and 611 (74.5%) who received combination platinum-based chemotherapy. The most common combination was carboplatin and paclitaxel. The median numbers of single-agent carboplatin and combination chemotherapy cycles were 5 and 6, respectively. Chemotherapy was evaluated as a time-varying covariate. After adjustment for demographic, disease, and treatment factors, the covariates significantly associated with survival included stage, extent of surgical debulking, and chemotherapy type. Single-agent carboplatin had a hazard ratio of 5.62 (95% CI 2.62-12.06) relative to combination chemotherapy.

Conclusion: In this population-based study, first-line combination chemotherapy was associated with improved survival compared to single-agent carboplatin in epithelial ovarian cancer. Higher rates of combination chemotherapy may improve outcomes at a population level.
Poster Session I

FIBROBLAST ACTIVATION PROTEIN REGULATES TUMOR-ASSOCIATED FIBROBLASTS AND EPITHELIAL OVARIAN CANCER CELLS

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The fibroblast activation protein (FAP) is a cell surface serine protease which has emerged as a specific marker of tumor-associated fibroblasts (TAFs). FAP has been shown to have both in vitro dipeptidyl peptidase and collagenase activity.

However, the biological function of FAP in the tumor microenvironment is largely unknown. In this study, we first show that TAFs isolated from ovarian cancer samples have the characteristics of stem cells. To explore the functional role of FAP, the protein was silenced by siRNA lentiviral vector transfection. FAP silencing inhibited the growth of TAFs in vitro, accompanied with cell cycle arrest at the G2 and S phase in TAFs. FAP silencing also reduced the stem cell marker gene expression in TAFs. SKOV3 cells do not express FAP. Although FAP-silenced SKOV3 cells induced ovarian tumors, the rate of tumor growth was significantly decreased, as shown in the xenograft mouse model. TAF phenotypes in the xenograft tumor tissues were further assayed by immunohistochemistry. The expression of TAF markers, including fibroblast-specific protein, FAP, smooth muscle actin, desmin, vascular endothelial growth factor and fibroblast growth factor was decreased in the tumor stroma induced by FAP-silenced SKOV3 cells. In conclusion, FAP is an important regulator of the microenvironment in tumor formation and targeting FAP is a potential therapeutic strategy to combat ovarian cancer.
Poster Session I

GENOME-WIDE DNA METHYLATION ANALYSIS IDENTIFIES PROGNOSTIC BIOMARKERS OF OVARIAN CANCER

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Objective: Abnormal DNA methylation contributes to tumorigenesis. The clinical significance of epigenetic effects in ovarian cancer is rarely explored. We aim to discover novel DNA methylation as a prognostic biomarker of ovarian cancer.

Methods: We did the methylomic analysis using bead arrays to in 46 malignant ovarian tumors. Bioinformatic analysis including the integration of gene-expression databases on the public domain revealed candidate gene lists. Verifications in vitro using RT-PCR and bisulfite pyrosequencing narrowed down the list to 3 genes. We did a comprehensive bisulfite pyrosequencing analysis of 3 genes in 116 ovarian cancer tissues and correlate the methylation patterns to clinicopathological features. Kaplan-Meier survival and Cox regression analysis estimates the competence of prognostic markers.

Result: Patients with high methylator phenotypes had a shorter progression-free survival (PFS) and overall survival (OS). Gene P methylation confers the most significant effects on OS with an adjusted hazard ratio of 7.24 (3.25 - 15.61) (P < 0.001). Patients with methylation of either gene N or H confers shorter PFS (9.1 vs 60.0 months for PFS; P < .001), whilst methylation of any two of these 3 genes had a shorter OS (22.2 vs 56.8 months; P < .001).

Conclusion: DNA methylation of gene P, N and H are associated with ovarian cancer survival. These DNA methylation may be biomarkers for individualized epigenetic therapy in the future.
MICRORNA PROFILING IN OVARIAN CANCER

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¹Obstetrics & Gynecology, St James’s Hospital & Trinity College, ²Gyneoncology, ³Medical Oncology, St. James’s Hospital, ⁴Histopathology, St James’s Hospital & Trinity College, Dublin, Ireland

Introduction: Ovarian cancer is the fifth most common cancer in women. There is a need for reliable diagnostic and prognostic markers for this disease. MicroRNAs are small, on average 22 nucleotide non-coding sequences of RNA, which control gene expression. MicroRNA profiling has allowed the identification of signatures associated with diagnosis, prognosis and response to treatment of human tumours. The aim of this study was to profile miRNAs from serum/blood of patients undergoing surgery for ovarian disease to determine if miRNAs have the potential to be used as diagnostic or prognostic markers in ovarian cancer. In addition the utility of miRNAs to be used as markers of chemotherapy response will be investigated.

Methods: Blood and serum collection is ongoing from all patients undergoing surgery for ovarian cancer and benign ovarian disease. Additional samples are being taken from patients undergoing chemotherapy for ovarian cancer. RNA extraction from serum/blood was optimised using a modified TRI Reagent® RT-Blood protocol. Profiling is being carried out using the TaqMan® array MicroRNA cards. A training set of 10 serous papillary ovarian adenocarcinomas and 10 benign serous cystadenomas have been analysed.

Conclusion: Initial analysis has yielded a panel of miRNAs expressed in a percentage of the malignant cases and not in any of benign cases. These include let-7a, miR 7, 130b, 142-5p, 324-5p, 190, RNU44 and 603. Validation will be carried out on a larger sample population. Analysis ongoing in chemo study.

Conclusion: miRNA signatures may improve detection and treatment of ovarian cancer.
Poster Session I

IS ROBOTIC-ASSISTED SURGERY A FEASIBLE OPTION FOR THE MANAGEMENT OF OVARIAN/TUBAL/PERITONEAL CANCER?

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Objective(s): Prospective feasibility evaluation of surgical outcomes of women with ovarian cancer undergoing robotic-assisted surgery

Study methods: During the first three years of the robotics program, data concerning patient demographics and surgical outcomes was collected prospectively on the cohort of all women who underwent robotic surgery for the management of ovarian cancer.

Results: Overall 32 patients had robotic surgical management with 14 patients receiving primary debulking and 18 patients receiving interval-debulking surgery after neoadjuvant chemotherapy. The mean age of women with primary debulking was 61 (range 44-88) and with interval debulking was 59 (range 24-87). Of those who had primary debulking, 57% were stage 3 or higher while in the neoadjuvant cohort 94% were stage 3 or more. The rate of optimal cytoreduction to less than 1cm of residual disease was 86% in those having primary surgical treatment and 100% in those who received neoadjuvant chemotherapy. Mean operative time was 293 minutes in primary surgery compared to 282 minutes in the interval-debulking cohort. Average hospitalization was 2.7 days in the primary debulking cohort compared to 2.2 days in the interval debulking group. With the exception of a perioperative mortality occurring in the first advanced ovarian cancer patient undergoing primary debulking, all other complications were rare and of little clinical significance.

Conclusion(s): At first glance, robotic surgery for the management of ovarian cancer whether in the primary or neoadjuvant setting is feasible and warrants further investigation as a surgical option.
Poster Session I

THE EFFECTIVENESS OF MISTLETOE IN THE TREATMENT ASPECT OF OVARIAN MALIGNANCY


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Objective: We planned to clarify the clinical effectiveness of Mistletoe during the chemotherapeutic treatment of patients with epithelial ovarian malignancy by evaluating the innate and acquired immune reactions.

Methods: We recruited the study group (n=16) who were diagnosed with epithelial ovarian malignancy and chiefly received platinum-based chemotherapy including either Mistletoe or control group (n=16). After treatment, blood sampling was performed 3 weeks interval for one-year and bloods were analyzed for absolute number of leukocytes, monocytes, lymphocytes, eosinophils, CD(cluster determinant)3, CD4, CD8, CD56, IL(interleukin)-2, IL-4, IL-12, TNF(tumor necrotizing factor)-α, and INF(interferon)-γ. The liver function tests were done in both group for evaluation of adverse effects.

Results: The absolute number of lymphocytes (p=0.0082) and natural killer (p=0.0008) cells were statistically increased in Mistletoe -treated group compared with non-treated group. There was statistically significant increments in the concentrations of CD3 (p=0.0096), CD4 (p=0.082) and CD8 (p=0.0012), but not in the absolute number of leukocytes and eosinophils. There was statistically significant increments in the concentrations of IL-2 (p=0.0112), IL-4 (p=0.0004), TNF-α (p=0.0140) and INF-γ (p=0.0001) in Mistletoe -treated group. But there were no significant differences in IL-12 between groups. There was not any notifiable adverse effect in the view of the liver function tests.

Conclusions: Mistletoe may reduce the hematologic side effects of antineoplastic drugs by improving the innate and acquired immunity and give patients with ovarian malignancy more effective chemotherapy ,and the results suggest that Mistletoe may be useful adjuvants in epithelial ovarian cancer patients treated with chemotherapeutic drug.
Poster Session I

INCIDENCE OF COEXISTING OVARIAN ENDOMETRIOSIS IN CLEAR CELL CARCINOMA AND ENDOMETRIOID CARCINOMA OF OVARY


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Objective: Ovarian clear cell carcinoma and endometrioid carcinoma may arise from endometriosis, but the molecular events have not been described precisely. We reviewed the pathologic reports for coexisting ovarian endometriosis in clear cell carcinoma or endometrioid carcinoma.

Method: A retrospective chart review was undertaken on pathologic report of the surgical specimen of the patients diagnosed with clear cell carcinoma or endometrioid carcinoma coexisting endometriosis from 2000 to 2012 in Asan Medical Center.

Result: Arising from endometriosis means that it transform endometriosis into ovarian cancer. Out of 94 clear cell carcinoma patients, 44(46.8%) had coexisting endometriosis and 23(52.2%) out of 44 patients arising from endometriosis. 24 patient(25.5%) out of 94 endometrioid carcinoma showed coexisting endometriosis and 16(66.7%) out of 24 patients arising from endometriosis. In clear cell carcinoma, half of them were associated with endometriosis and 52.2% cases showed arising from endometriosis. In endometrioid carcinoma, the lesser number of case were associated endometriosis but much more cases appeared arising from endometriosis.

Discussion: Many of clear cell carcinoma and endometrioid carcinoma had in company with endometriosis. Amusingly, many of them were arising from endometriosis.

Until now, we are difficult to say endometriosis is precancerous lesion. But in our study, we observe many of clear cell carcinoma and endometrioid carcinoma were transformed from endometriosis.

For that reason, we are currently undertaking a study in these patients to clarify molecular mechanisms of the possible transformation from ovarian endometriosis to ovarian clear cell carcinoma or ovarian endometrioid carcinoma.
Poster Session I

POTENTIAL MONOCLONAL ANTIBODY THERAPY FOR THE TREATMENT OF OVARIAN CANCER

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Two pan-cancer markers, CA215 and GnRH receptor, were found to be highly expressed on the surface of cancer cells of many human tissue origins including those of the ovary. Two monoclonal antibodies (Mabs), RP215 and GHR106, were developed to recognize these two antigens, respectively. RP215 was found to react with carbohydrate-associated epitope of the cancer cell-expressed immunoglobulin superfamily proteins, known as CA215, while GHR106 was found to react with the extracellular domains of human GnRH receptor.

Preclinical evaluations of RP215 and GHR106 as potential Mab-based anti-cancer drugs were performed for the treatment of ovarian cancers.

MALDI-TOF MS analysis, immunohistochemical studies (IHC), Western blot assays, in vitro apoptosis assay, complement-dependent cytotoxicity (CDC) assay, and in vivo nude mouse experiments were conducted. Three ovarian cancer cell lines, OC-3-VGH, OVCAR-3 and SKOV-3 were selected as experimental models.

IHC with tissue sections of ovarian cancer revealed that the positive staining rates with RP215 could be as high as 64.4% (56/87). These two Mabs or their chimeric forms were highly effective in inducing apoptosis and CDC reactions to ovarian cancer cells. Furthermore, in vivo nude mouse experiments with implanted OC-3-VGH cancer cells revealed significant dose-dependent inhibition of the growth of tumor cells by RP215. In addition, GHR106 functions like long-acting GnRH analogs in its biological actions to cancer cells.

The results presented in this study should provide a strong basis for these two Mabs to be further developed as anti-cancer drugs which might potentially target the ovarian cancer as well as others in humans.
EXTRACT MARSDENIA IN COMBINATION WITH HYPERTHERMIA ON PROLIFERATION AND CEACAM6 EXPRESSION OF THE HUMAN OVARIAN CANCER CELL LINE SKOV3

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Objective: To investigate the effect of Extract Marsdenia in combination with hyperthermia (42 °C) on cell proliferation and expression of carcinoembryonic antigen-related adhesion molecule 6 (CEACAM6) mRNA in ovarian cancer SKOV3 cell line in vitro.

Methods: Cell growth inhibition was evaluated by MTT assay, apoptosis was measured by flow cytometry (FCM), and carcinoembryonic antigen-related adhesion molecule 6 (CEACAM6) mRNA was assessed by qRT-PCR.

Results: Extract Marsdenia and hyperthermia (42°C) significantly inhibits tumor cell proliferation, induces tumor cell apoptosis, and inhibits expression of CEACAM6 mRNA expression in tumor cell, which was in a concentration dependent manner and is enhanced by hyperthermia. There is significant statistics difference between experiment group and control group (p< 0.05).

Conclusion: Extract Marsdenia in combination with hyperthermia (42°C) significantly inhibits tumor cell proliferation, induces tumor cell apoptosis, and down-regulate expression of carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6). mRNA, providing a certain theoretical basis for looking new ways of ovarian cancer clinical treatment.
Poster Session I

A SINGLE SURGEON’S INITIAL EXPERIENCES FOR EXTENSIVE CYTOREDUCTIVE SURGERIES (CRS) IN HIGH RISK PERITONEAL CANCER

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Objective: This retrospective study is to investigate the feasibility and short-term surgical outcome of a single surgeon’s initial experience of extensive CRS for high risk peritoneal malignancies after completion of 3 years fellowship program (≥2 CRS/weeks during fellowship program).

Methods: Medical records for 50 women who underwent explorative laparotomy for suspicious peritoneal malignancy between Jul 2010 and Mar 2012 were retrospectively reviewed. Seven secondary, 2 tertiary, and 1 quinary cytoreductive surgeries were performed for the recurrent disease.

Results: Upper abdominal procedures (23/29, 79.3%) including diaphragmatic stripping and/or resection, splenectomy, distal pancreatectomy, cholecystectomy, suprarenal lymph node dissection (LND), celiac axis LND, mesenteric LND, adrenalectomy, liver wedge resection, or hemicolecction resulted in 69% (20/29) of complete cytoreduction (microscopic residual tumor) and 97% (28/29) of optimal cytoreduction (residual tumor ≤1cm). Eight of the 9 women with visible residual tumor had less than 5mm sized tumor. The causes to remaining residual tumor are mainly surgical and/or technical limitation [for small bowel mesentery (n=6), celiac axis (n=2), and mesenteric LN (n=1)] and long operation time and/or patients’ general condition [diaphragm (n=1) and suprarenal LN (n=1)]. Grade 3 or 4 morbidities requiring intervention or reoperation were identified in 4 patients (13.8%).

Conclusion: This is the first report to reveal that favorable surgical outcome might be expected even in quite challenging peritoneal cancers from an initial surgical series of gynecologic oncologists who completed sufficient training of extensive CRS with adequate mentoring.
Poster Session I

EARLY MORTALITY AFTER CYTOREDUCTIVE IN EPITHELIAL OVARIAN CANCER: CAUSE AND PREVENTIVE STRATEGY

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Objective: We investigated early mortality after cytoreductive surgery and adjuvant chemotherapy to make strategies to improve treatment outcomes in epithelial ovarian cancer in hospital with high rate of optimal debulking (96% of optimal cytoreduction and 79% of optimal cytoreduction) and favorable survival (Median PFS, 17mo; Median OS, not reached, estimated more than 70 months).

Method: Medical record of 393 patients with epithelial ovarian cancer was retrospectively reviewed.

Results: No early mortality was identified in early ovarian cancer (n=104). Of 289 patients with stage IIIc and IV, 20 mortalities were identified less than 10 months after cytoreductive surgery. In order of frequencies, febrile neutropenia related infection (n=6; with pneumonia, septic shock, and ARDS), disease progression even with scheduled chemotherapy (n=6), unknown due to follow up loss (n=5; might be traffic accident, chronic illness-related event, suicide etc.), postoperative ileus related event (n=2), and venous thromboembolism related event (n=1) were identified. Prophylactic use of G-CSF in patients with high risk of febrile neutropenia, adequate thromboprophylaxis, and education for the importance of adjuvant chemotherapy and OPD follow up might reduce the early mortality in advanced epithelial ovarian cancer.

Conclusion: The proportion of early mortality after cytoreductive surgery and adjuvant chemotherapy is quite significant. Better strategies including prophylactic use of G-CSF and adequate thromboprophylaxis in high risk patients are required.
Poster Session I

SURVIVAL OUTCOMES AFTER PRIMARY DEBULKING SURGERY (PDS) AND NEOADJUVANT CHEMOTHERAPY (NAC) IN BULKY STAGE IIIC AND IV OVARIAN

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Objective: The purpose of the current study is to investigate the survival outcome of ovarian cancer treated at National Cancer Center Korea.

Methods: Indication for NAC is

① Poor performance status,
② Extra-peritoneal disease (except isolated malignant pleural effusion & cardiophrenic LN metastasis),
③ Involvement of the mesenteric root of the small intestine,
④ Multiple liver parenchymal metastasis requiring total resection of liver, and
⑤ Pancreatic head metastasis.

Old indication for NAC includes

① Involvement of the porta hepatis and celiac axis,
② Para-aortic lymph node metastasis above the renal veins, and
③ Disease that is larger than 2 cm and perforates the diaphragm.

After NAC, all traces of regressed metastatic ovarian cancer were removed to minimize the potential risk of remaining chemotherapy-resistant cell, potential ovarian cancer stem cells.

Results: Of 279 eligible patients with stage IIIc and IV, 143 (51%) underwent PDS and 136 (49%) received NAC. Median age was 55 years. Main histology was serous histology (212, 76%). Complete cytoreduction (microscopic residual tumor) and optimal cytoreduction (residual tumor < 1cm) were achieved in 79% and 96% of the patients, respectively. The median progression free survival (PFS) was 17 months. And overall survival (OS) was not reached, but estimated more than 70 months.

Conclusion: Complete removal of all visible and palpable tumors and traces of regressed metastatic ovarian cancer after NAC results in the best survival outcomes. Research on removing all traces of regressed metastatic ovarian cancer is needed to know the real benefit of such surgical strategy.
CLINICAL CHARACTERISTICS OF MALIGNANT BRENNER TUMORS OF THE OVARY

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Background: Malignant Brenner tumors are rare, malignant, epithelial tumors of the ovary. Because of the low incidence of these tumors, information on prognosis, development of metastases, chemosensitivity and recurrence is scarce. Therefore, treatment is similar to other epithelial ovarian cancers. Possibly less extensive treatment is sufficient because it has been reported that malignant Brenner tumors behave less aggressive.

Aim: To investigate the incidence, clinical characteristics and prognosis of malignant Brenner tumors to evaluate optimal treatment.

Methods: We retrospectively analysed files of all patients diagnosed with a Brenner tumor between 1990 and 2010 in the Netherlands, using the Dutch nationwide registry of pathology (PALGA). Data on course of disease and outcomes were recorded.

Preliminary results: There were 3778 records in PALGA. The majority were benign tumors. Also tumors of borderline malignancy occurred. Finally, 104 patients had a malignant Brenner tumour. Patients were treated in referral hospitals (n=85) and in general hospitals (n=114). Not all patients have been completely analysed yet. Their median age was 59 years. Fifty percent of the patients presented in FIGO stage I, and 50% with FIGO stage III disease. Sixty three percent had a disease free survival ranging from 2 to 9 years and 38% died of disease.

Conclusion: This study is the largest study on malignant Brenner tumors. This specific type of ovarian cancer should be treated similar to other epithelial ovarian cancers until more data are available that show a less malignant behaviour.

[Macroscopic image of malignant Brenner tumor.]
Poster Session I

A TUMOR-STROMA TARGETED ONCOLYTIC ADENOVIRUS TO TREAT OVARY CANCER


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Aim: Targeting the ovarian tumor stroma in addition to the malignant cell to achieve complete tumor regression.

Methods and results: In this work, we modified a previously designed tumor stroma-targeted conditionally replicative adenovirus based on the SPARC promoter by introducing a mutated E1A unable to bind pRB and pseudotyped the virus with a chimeric Ad5/3 fiber (AdF512v1); we assessed its replication/lytic capacity in ovary cancer in vitro and in vivo. AdF512v1 was able to replicate in fresh samples obtained from patients:

a) with only primary tumor (n=4);

b) that underwent neoadjuvant treatment (n=5);

c) with metastatic disease (n=2).

In addition, we assessed the efficacy, biodistribution and clearance of AdF512v1 by using human ovary cancer cells injected i.p. We found that the tumor is more efficiently infected that liver or spleen and by day 18 we can still find the virus in the tumor but not in the liver. We show that four i.p. injections of 5 x 10^10 v.p eliminated or reduce tumor growth in all the mice. Moreover, AdF512v1 replication in tumor models was enhanced 15 to 40 fold when the tumor contained a mix of malignant and SPARC-expressing stromal cells. Contrary to the wild type virus, AdF512v1 was unable to replicate in normal human ovary samples (n=5).

Conclusion: This study provides evidence on the lytic capacity of this CRAp and highlights the importance of targeting the stromal tissue in addition to the malignant cell compartment to achieve tumor regression.
Poster Session I

IN VITRO CHEMORESPONSE ASSESSMENT OF OPTIMALLY AND SUBOPTIMALLY DEBULKED PRIMARY OVARIAN CANCER

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Background: Primary ovarian cancer (POC) patients who have been optimally debulked (defined as 1 cm or less residual tumor) have better prognosis compared to suboptimally debulked patients. An understanding of the differences in tumor biology between suboptimally and optimally debulked patients is lacking.

Objective: Determine whether in vitro chemoresponse differs between optimally and suboptimally debulked POC patient specimens.

Methods: Patients enrolled in a post-market clinical study for whom data on surgical debulking status were available were retrospectively identified. POC patient specimens were tested for response to twelve drugs or drug combinations using an in vitro chemoresponse assay. Specimens were classified as responsive or non-responsive based on dose response curves.

Results: 821 optimally and 171 suboptimally debulked patients were identified. The percentage of specimens testing non-responsive to all drugs significantly differed according to debulking status (optimal, 13.8%; suboptimal, 23.4%; p=0.002). There was also a statistically significant difference in the percentage of responsive specimens according to debulking status for the carboplatin/docetaxel combination (optimal, 82.2%; suboptimal, 70.3%; p< 0.01). Similar comparisons for other platinum and/or taxane-based drug combinations trended towards significance (paclitaxel, 60.8% vs. 52.8%, p=0.11; carboplatin/paclitaxel, 78.7% vs. 72.3%, p=0.13; carboplatin, 62.0% vs. 54.5%, p=0.13; carboplatin/gemcitabine, 78.0% vs. 71.5%, p=0.14).

Conclusions: In vitro chemoresponse profiles of optimally and suboptimally debulked POC differ. These results suggest that the inherent biology of suboptimally debulked tumors may contribute to increased chemoresistance and poorer patient prognosis.
IDENTIFICATION OF MIRNAS AND THEIR TARGET GENES INVOLVED IN OVARIAN CANCER METASTASIS

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Objectives: Aberrant expression of microRNA (miRNA) has been implicated in ovarian carcinoma. However, roles of miRNA in ovarian caner metastasis remains unknown. This study is aimed to identify differentially expressed miRNAs in paired SKOV-3ip and SKOV-3 cells and their target genes involved in ovarian cancer metastasis.

Methods: We examined the distinct miRNA expression profiles between paired high-metastatic human serous ovarian cancer cell SKOV-3ip and low-metastatic human serous ovarian cell SKOV-3 using miRNA microarray. Subsequently, Real-time RT-PCR was performed to confirm the differential expression level of miR-22 in both cell lines and clinical samples, followed by functional study on miR-22.

Results: Through a screen with microarray, we found 43 miRNAs differentially expressed between SKOV-3ip and SKOV-3 cells. Among these candidates, 11 miRNAs (including let-7f, miR-22, and miR-31 et al.) were downregulated and 32 miRNAs (including miR-1284, miR-1264, and miR-923 et al.) upregulated in SKOV-3ip cells compared with SKOV-3 cells. Specifically, validation by Real-time RT-PCR indicated miR-22 was negatively correlated with the metastatic potential of ovarian cancer cells. Meanwhile, decreased miR-22 expression was also observed in ovarian cancer tissues relative to benign ovarian tumors. Furthermore, functional studies uncovered an inhibitory effect of miR-22 on migration and invasion of ovarian cancer cells, and a negative regulation on Tiam1, a well-characterized pro-metastatic gene in various cancers including ovarian cancer.

Conclusions: Our findings suggested that miR-22 might inhibit ovarian cancer metastasis by targeting Tiam1 and miRNA may play an important role in ovarian cancer metastasis.
Poster Session I

CAN NODAL SAMPLING AND PERITONEAL BIOPSIES OMITTED IN STAGE I OVARIAN CANCER? A STUDY OF CLINICAL PRACTICE IN SOUTH-WALES

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Background: In Wales the incidence of ovarian cancer is 26.1 per 100,000. Unlike FIGO recommendations, All Wales Guideline 2000 recommend includes TAHBSO, omentectomy and peritoneal washing. Nodal dissection is done only if clinically or radiologically indicated.

Methods: Retrospective data analysis of patients with FIGO stage 1 ovarian cancer from 2004-10. The two centres in South-Wales follow the same guidelines for epithelial ovarian cancer (EOC). We reviewed the relapse and overall survival rates.

Results: A total of 269 patients were recorded as FIGO stage 1 and 116 patients were included in the final analysis (153 were non-EOC). Median age of patients was 63 years (32-88) and median follow-up period was 41 months (12-95). 18 patients had relapse (15.5%), of these 17 patients had high risk factors. In relapsed patients, median age was 58 years (range 38-76). 6/18 patients died of unrelated causes. 18 patients who were not offered chemotherapy had stage Ia grade I EOC without high risk factors. Their median age was 64 years (33-82). These were the patients (15.5% of the total) who were potentially undertreated because of the lack of systematic nodal sampling and peritoneal biopsies, which could have resulted in an indication for chemotherapy if positive. One of the 18 patients who did not receive chemotherapy relapsed and died. 95/116 (81.9%) patients had other reasons for chemotherapy.

Conclusion: FIGO staging in our series could have changed the management in 1/116 (0.86%), could have resulted in better prognostications at the cost of increased peri-operative morbidity. The overall survival rate is comparable to many published studies.
Poster Session I

RISK OF MALIGNANCY INDEX IN WOMEN WITH ADNEXAL MASSES - COMPARING RMI 1, 2 AND 3 IN THE WELSH POPULATION

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Introduction: Ovarian cancer remains a leading cause of mortality among women in the developed world. The purpose of this retrospective study is to evaluate the RMI in triaging women with pelvic masses in Wales.

Methods: A retrospective review of 328 patients was performed using the Trust's database of patients with pelvic masses discussed at the Gynaecological-Oncology Multidisciplinary Meeting over an 18-month period. 81 charts did not have the required parameters to calculate RMI, leaving a total of 247 for review. The three versions of RMI were compared. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CA-125 levels only and the RMIs were calculated.

Results: Of the 247 patients, 160 had benign ovarian lesions while 87 were diagnosed with malignant masses. The sensitivity and specificity of CA-125 at 35kU/L are 76% and 67% respectively. CA-125 was found to be a relevant predictor of malignancy. However, the area under the ROC curve for each of the RMIs was greater than the area for CA-125 only. At a threshold of 200, the sensitivities of RMI 1, 2 and 3 are 66%, 74% and 68% respectively while the specificities are 91%, 79% and 85% respectively.

Conclusion: This is the first study in Wales to evaluate RMI 1, 2 and 3. Overall, RMI 1 and 2 appear to be better malignancy predictors than RMI 3. It would be recommended that RMI 1 and 2 be compared in a head-to-head prospective study. This is already ongoing in Singleton Hospital, Swansea, UK.
Poster Session I

THE IMPACT OF AGE ON FIRST LINE CHEMOTHERAPY AND SURGICAL TREATMENT OF EPITHELIAL OVARIAN CANCER

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Introduction: Standard treatment for epithelial ovarian carcinoma (EOC) is combination of surgery and chemotherapy. Most commonly used first-line drugs are carboplatin and paclitaxel (C/P). Decisions involving elderly are complex and single agent carboplatin (C) is often preferred. We analysed the toxicity profile and outcome for elderly patients treated first line with both: C/P and C alone.

Methods: A retrospective analysis of 82 elderly patients (>75 years) treated between April 1996 and October 2009 was performed. Age, co-morbidities, CA-125 at diagnosis, histology, stage, outcome of cytoreductive surgery (CRS), chemotherapy regimen, toxicity and clinical response were recorded.

Results: The majority, 76%(63/82) of patients had serous EOC with 58.5% presenting as FIGO stage 3c, median CA-125 of 340.2 U/ml (range: 5-5702). 67.1%(55/82) had CRS with 61.9%(34) optimally debulked. 84.2% of patients (69/82) received chemotherapy and were therefore evaluable for the purpose of this analysis. 94.2%(65/69) completed treatment (mean number of cycles = 5.1). 35.4%(23/65) received C/P and 63.1%(41/65) received single agent C. The commonest complication was peripheral neuropathy - 56.5% (13/23) in combination arm. There were 35 dose delays - 34.6%(9/26) C/P and 60.4%(26/43) C. Median survival was 21.3 months. Median PFS was 8.8 months in C/P arm and 7 months in the C arm (95%CI-0.71 to 1.8-not statistically significant).

Toxicity of treatment with C/P is comparable to single agent C in elderly population with frequent dose delays and dose reductions. Initial assessment of comorbidities and performance status is essential however effort should be made to offer patients optimal treatment with C/P.
Poster Session I

DVD-BASED GENETIC COUNSELLING IS AS EFFECTIVE AND MORE COST-EFFICIENT THAN STANDARD-COUNSELLING FOR BRCA TESTING: RESULTS FROM A RANDOMISED TRIAL

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Aim: To compare standard individual genetic counselling for BRCA testing with a DVD-based approach.

Methods: Genetic counselling clinics within the GCaPPS trial (Feb-2009 to July-2010) were randomised to standard individual and DVD-based approaches. The latter involved a special DVD presentation followed by a face-to-face counselling session. The counselling time was documented. Knowledge (baseline and post-counselling) was assessed by a 10-item questionnaire, and counselling satisfaction by the GCSS scale. Another questionnaire assessed relevance, satisfaction, adequacy, emotional impact and improvement of understanding with the DVD. A cost minimisation analysis was undertaken for the two counselling approaches.

Results: 936 people underwent genetic counselling (individual=527; DVD-based=409). Characteristics of the two groups were similar at baseline. Participants mean age was 53.9(S.D 15) years. 66.8% were women and 33.2% men. Type of counselling did not affect genetic testing uptake (p=0.411). Counselling increased knowledge scores (p<0.0005). The two counselling approaches did not differ in counselling satisfaction (p=0.468) or in levels of increased knowledge (p=0.174). The DVD-based approach significantly reduced counselling time (45(IQR,5) min) compared to the individual approach (20(IQR,10) min) (p<0.0005). 98% found information provided and DVD length satisfactory. 85-89% reported improved understanding of risks, benefits, implications and purpose of genetic testing. 95% would recommend this to others. The cost of DVD-based counselling was £7,787 and of the individual approach was £17,307 (cost saving=£9,520). DVD led to a cost minimisation per volunteer counselled of £14.

Conclusions: DVD-based counselling is an effective, acceptable, equivalent and a more cost efficient alternative to traditional individual counselling.
Poster Session I

RECURRENT GRANULOSA CELL TUMORS OF THE OVARY (GCTS) : A MITO-9 RETROSPECTIVE STUDY


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Background and aims: Optimal treatment of recurrent GCTs is unknown. The aim of this study was to evaluate characteristics and treatment of recurrent GCTs.

Methods: Data concerning 35 recurrent GCTs treated at MITO centers were reviewed.

Results: FIGO stage was: 11 IA, 11 IC, 6 Ix, 1 IIB, 5 IIIC and 1 IV. All patients had undergone primary surgical treatment, plus adjuvant chemotherapy in 7 cases. The median recurrence free survival was 53.2 months with difference between patients receiving adjuvant chemotherapy (72.5 months) and not (48 months) and between patients with surgical staging (47 months) and without (64.5 months). Recurrence sites were: pelvic, 13; abdominal, 6; lymph-nodal 2; pelvic+ abdominal, 7; abdominal+lymph-nodal, 4; pelvic+ lymph-nodal, 3. Twenty-five patients underwent debulking surgery+chemotherapy, 7 surgery, 1 surgery+radiotherapy, 1 chemotherapy and 1 palliation. 69% of patients completed chemotherapy. No difference was found in OS among patients receiving or not chemotherapy at recurrence and among sites. Eleven patients developed a second relapse after a median time of 38 months. 81.8% had received chemotherapy at first recurrence. Four patients underwent surgery, 4 surgery+chemotherapy, 1 surgery+radiotherapy and 2 palliation. Four patients developed a third recurrence after a median time of 41 months. Two patients received chemotherapy and 2 hepatic resection+thermo-ablation. Nine patients (25.7%) died of disease (11.4%, 30%, 50% at first, second and third relapse, respectively). 10y-OS was 87.6% and 71% for I and advanced stage, respectively (p< 0.05).

Conclusions: Patients should always be treated in case of recurrence. Surgery remains the cornerstone at relapse.
Poster Session I

USE OF KPT-SINE (SELECTIVE INHIBITORS OF NUCLEAR EXPORT) IN OVARIAN CANCER MODELS: OVERCOMING CISPLATIN RESISTANCE AND PROLONGATION OF SURVIVAL

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Ovarian cancer (OvCa) is the most lethal female reproductive tract malignancy worldwide with >190,000 new cases diagnosed yearly. Overall, ~60% of patients will relapse after primary therapy and for the majority of women with advanced disease, their cancers are currently incurable. New therapeutic approaches/strategies are needed.

During the course of OvCa evolution, multiple tumor suppressor proteins (TSPs) are inactivated by cytoplasmic mislocation. Chromosomal region maintenance 1 (CRM1, also known as XPO1/exportin 1) is solely responsible for the nuclear export of the major TSPs, and increased CRM1 expression has been linked to advanced OvCa stage and poor overall survival. To address the therapeutic role of CRM1 inhibition in OvCa, we tested two novel selective inhibitors of nuclear export (SINEs) in vitro and in vivo.

For in vitro studies, we used KPT-185 as a single agent and in combination with cisplatinum in the isogenic cell lines A2780 and CP70. In both lines, combination treatment demonstrated an additive effect on cell death and overcame cisplatinum resistance. The use of the orally bioavailable KPT330 as a single agent in an in vivo Rag1 KO mouse model, using patient-derived chemonaive cell lines, resulted in both inhibition of subcutaneous tumor growth and markedly increased survival. In control mice, shifting to treatment with KPT330 resulted in tumor growth arrest.

Together, these studies demonstrate successful first use of specifically-designed, potent and irreversible CRM1 inhibitors in OvCa on overcoming cisplatin resistance in vitro and prolonging survival in an animal model. First-in-man trials are planned to start Summer 2012.
Poster Session I

ENDOMETRIAL ATYPICAL HYPERPLASIA IN SEROUS OVARIAN CANCER: IS THERE ANY RELATIONSHIPS?

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Background: The prevalence of ovarian cancer is sharply increased in developed and developing countries lately, in which Serous Epithelial Ovarian Cancer (SOC) is the most frequent histological type. There has been a new argument that the origin of SOC could be in endometrial or fallopian tube, not in the ovary itself. Endometrial Atypical Hyperplasia (EAH) is a risk factor for endometrial cancer, and it is not known if this lesion could induce ovarian cancer by some mechanism. P53 and E-cadherin genes play an important role in ovarian cancer as well as endometrial cancer, thus they could be used to observe the relationships between ovarian cancer and endometrial atypical hyperplasia in order to elucidate the origin and pathogenesis of ovarian cancer.

Aim: To analyze the relationships between P53 and E-cadherin expression in ovarian cancer patients who has endometrial atypical hyperplasia.

Method: Immunohistochemistry analysis using monoclonal antibody of P53 and E-Cadherin to observe the expression of these proteins in 54 ovarian cancer and endometrial atypical hyperplasia tissues.

Result: Expression of P53 was found to increase in SOC especially for the poorly differentiation tumor (p = 0.001) and this expression was also has strong relation to the expression of P53 in EAH (p = 0.000). The expression of E-cadherin was also increase in SOC especially poorly differentiation (p = 0001) and has significantly relation to its expression in EAH (p = 0.017).

Conclusion: Endometrial atypical hyperplasia has relationships with Serous Ovarian Cancer.
Poster Session I

LOW SERUM CREATININE AND THE 1ST CYCLE HEMATOLOGICAL TOXICITIES IN PATIENTS WITH OVARIAN CANCER TREATED BY DOSE DENSE TC

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Background: Dose dense TC (ddTC) is a novel standard therapy for patients (pts) with advanced ovarian cancer, although hematological toxicities (hemTX), especially anemia, may increase as observed in NOVEL trial (JGOG3016). Low serum creatinine (LCr), especially below 0.7 mg/dl, may lead to overestimation of GFR. GOG announced that pts with LCr should use a minimum value of 0.7 mg/dl to estimate GFR. The correlation between LCr and hemTX treated by ddTC is unknown.

Methods: GFR was determined using the Cockcroft-Gault formula. Serum creatinine concentrations were measured using enzymatic assays. Minimum value of 0.7 mg/dl was not used during this period of time. The carboplatin dose was then calculated by Calvert equation. HemTX were defined as, Grade 3 or 4 (by CTC-AE ver.4) neutropenia, anemia, and thrombocytopenia. Using electrical chart, frequency of hemTX in the 1st cycle, delay of 2nd cycle due to hemTX and correlations between serum creatinine (less than 0.7 or not) were examined.

Results: From Feb. 2010 to Dec. 2011, 61 consecutive pts were treated with ddTC. LCr was observed in 73% of pts. Among 61 pts, 20 (33%), 8 (13%), and 2 (3 %) pts experienced Grade3/4 neutropenia, anemia, and thrombocytopenia, respectively in the 1st cycle. HemTX in pts with LCr and the others were as in Table 1.

<table>
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<tr>
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<th>G3/4 hemTX</th>
<th>2nd cycle delay due to hemTX</th>
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<tbody>
<tr>
<td>Pts with LCr (n=45)</td>
<td>18 (40 %)</td>
<td>14 (31 %)</td>
</tr>
<tr>
<td>Pts without LCr (n=16)</td>
<td>6 (38 %)</td>
<td>5 (32 %)</td>
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[Correlation between LCr and hemTX]

Conclusions: LCr is frequent in Japanese female pts. LCr doesn't seem to affect hemTX in the 1st cycle. The rationale using a minimum value of 0.7 mg/dl should be further studied by larger population, such as NOVEL trial.
ABERRANT ACTIVATION OF SPLEEN TYROSINE KINASE IN OVARIAN CANCER IDENTIFIED THROUGH A GLOBAL PHOSPHORYLATION PROFILING OF PROTEIN TYROSINE KINASES

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Objectives: Aberrations in protein kinase activity and the consequent deregulation of downstream signaling pathways are considered a hallmark of oncogenesis. We investigated the phosphorylation state, the ultimate readout of dysregulated activity, of protein tyrosine kinases in ovarian tumors.

Methods: An innovative Luminex multiplex platform was employed to systematically determine phosphorylation status of protein tyrosine kinases in a total of 69 protein lysates derived from normal human ovarian surface epithelial (HOSE) cells, ovarian tumors, and cancer cell lines. Significance Analysis of Microarrays (SAM) was performed to identify the signature of phosphorylated kinases with statistical significance. Profiling results were confirmed by using phosphor-specific kinase antibodies in immunoblot analysis of the profiled lysates and immunohistochemistry on formalin-fixed paraffin-embedded archived ovarian and fallopian tissues, as well as immunofluorescence of ovarian cancer cells growing as monolayer or 3D Matrigel cell cultures.

Results: A signature of twenty-two phosphorylated protein tyrosine kinases was identified by SAM analysis of the profiling data. Spleen Tyrosine Kinase (SYK), a novel tyrosine kinase included in the signature, was found significantly phosphorylated in lysates from ovarian cancer tissues compared to normal tissues by both Western blot analysis and immunohistochemistry on 94 clinical ovarian tissues (P=0.024). SYK phosphorylation was also identified in tubal intraepithelial carcinomas, the hypothesized precursors of high-grade serous ovarian carcinomas. However, SYK activation was not observed in ovarian cancer cell lines growing as attached monolayer cells, but was present when they grew as mouse xenografts or in 3D Matrigel in vitro cultures.

Conclusions: We are the first to report that SYK, an extensively investigated tyrosine kinase in hematopoietic cells, is aberrantly phosphorylated and activated in ovarian cancer. SYK phosphorylation in ovarian cancer might be induced by extracellular stimuli that are exclusively present in the tumor microenvironment. These findings provide additional options in targeted therapy for ovarian cancer.
Poster Session I

IS INTRAPERITONEAL CHEMOTHERAPY EFFECTIVE IN TREATING WOMEN WITH STAGE IIIC OVARIAN CARCINOMA BY RETROPERITONEAL NODAL METASTASIS?

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Objective: Intraperitoneal (IP) chemotherapy has been shown to improve survival of women with stage IIIC ovarian carcinoma as compared to intravenous (IV) chemotherapy. The objective of this study is to examine the effectiveness of IP chemotherapy in patients with stage IIIC disease by retroperitoneal nodal metastasis.

Methods: This is a retrospective cohort study of patients with stage IIIC ovarian carcinoma treated with IV or IP chemotherapy between 2004-2010. Data were collected, Kaplan-Meier curves generated and multivariate analyses performed.

Results: Of 393 patients with advanced stage ovarian carcinoma, 202 had optimally cytoreduced stage IIIC disease. Of those patients, 95 received IV chemotherapy and 114 received IP chemotherapy. 20 patients had stage IIIC disease due to retroperitoneal lymphnode involvement- 10 received IV chemotherapy and 10 received IP chemotherapy. Survival was superior in all women treated with IP chemotherapy as compared to IV chemotherapy (p= 0.004). Patients with stage IIIC disease by abdominal involvement or stage IIIC disease by retroperitoneal nodal involvement who were treated with IP chemotherapy had equivalent survival (p=0.34). Patients with stage IIIC disease by retroperitoneal nodal involvement had improved survival if they were treated with IP chemotherapy as compared to IV chemotherapy (p= 0.04).

Conclusion: IP chemotherapy appears equally as effective in patients with stage IIIC ovarian carcinoma due to retroperitoneal nodal metastasis as it is in patients with stage IIIC ovarian carcinoma due to abdominal metastases. Women with stage IIIC disease by retroperitoneal nodal involvement experienced improved survival when treated with IP chemotherapy as compared to IV chemotherapy.
**Poster Session I**

**OVARIAN CANCER TREATMENT IN PATIENTS OVER 65 YEARS**

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Backgrounds and aims: The cornerstone of treatment of ovarian cancer is cytoreductive surgery followed by platinum-based chemotherapy.

The optimal treatment of women with advanced age is unclear. This study analyzes our experience in treating ovarian cancer in two different periods.

**Material and methods:** We identified patients with ovarian cancer aged 65 and over, treated in the HMI of Granada from 1990-2010, with a total of 93 patients.

We analyzed two periods 1990-2000 and 2001-2010 and the following data, age, age at menopause, clinical stage, surgery, chemotherapy (monochemotherapy and chemotherapy).

**Results:** We identified 93 patients with a mean age of 72.39 (65-98).

In group I the mean age was 72.44 and 72.36 in group II, no statistical differences.

The age of menopause is 49.76 and 49.85 respectively, without statistical differences.

Clinical stage (I-II) is 33.3% and 40.7% in group II with no statistical differences.

Surgery was performed in 65.78% of group I and 85.45% in group II (p = 0.0402).

The chemotherapy was 52.63% and 70.90% (p = 0.0109).

Single agent chemotherapy was used in 40% of patients (group I) and 12.82% (group II), while polychemotherapy in 60% of group I and 87.18% of group II.

**Conclusions:** Age alone should not limit access to treatments.

We have improved surgical treatment and chemotherapy.

We have improved the diagnosis.
Poster Session I

HIGH PREVALENCE OF ENDOMETRIAL LESIONS IN WOMEN WITH EPITHELIAL OVARIAN CARCINOMA


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Objective: Accumulating evidence has been gathered indicating the Müllerian ducts as the origin of serous epithelial ovarian carcinoma (EOC). Precursor lesions have been identified in the fallopian tubes. Recently, the endometrium has been suggested to be a putative source for precursor lesions of serous EOC. The aim of the present study is to review the endometrium from a large cohort of women with serous EOC in order to reveal the prevalence of endometrial lesions in these women.

Methods: In total, 101 women with serous EOC were retrospectively selected and all endometrial and ovarian slides were extensively reviewed by two pathologists. The endometrium was scored for intraepithelial carcinoma, hyperplasia with or without atypia or other endometrial lesions. Clinicopathological variables were retrieved from medical and operative records.

Results: The endometrium was without lesions in 46%. In 41 cases (41%) hyperplasia was identified in the endometrium, with synchronous atypia in nineteen cases (19%). Atypia without concordant hyperplasia was identified in two cases (2%) and endometrial intraepithelial carcinoma in 7 (7%). In four cases (4%) a second primary endometrial carcinoma was present: two cases with endometrioid carcinoma, one rhabdomyosarcoma and one carcinosarcoma.

Conclusion: Endometrial lesions showed common in women with serous EOC and should be taken into account when managing treatment options. Yet, a possible role in the origin of EOC is unknown and should be explored further to reveal its impact on ovarian cancer screening. Meanwhile, a hysterectomy is strongly recommended in these women or at least a curettage should be offered.
Poster Session I

A NOVEL PLASMA AMINO ACID PROFILE-BASED BIOMARKER FOR GYNECOLOGIC CANCER USING ‘AMINOINDEX TECHNOLOGY’

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Objectives: It is known that plasma free amino acid (PFAA) profile is usually maintained at a constant level in healthy individuals, but various diseases including cancer could change PFAA profile. In this multicenter study, we create and evaluate the performance of plasma amino acid profile for detection of all three gynecologic cancers: cervical, endometrial, and ovarian cancer.

Methods: Plasma samples were obtained from individuals diagnosed as either ovarian cancer (N=113), endometrial cancer (N=189), cervical cancer (N=211) and benign gynecologic disease (N=305), and healthy control (N=1631). Plasma amino acid concentrations were measured by liquid chromatography and mass spectrometry (LC-MS). For multivariate analysis, we create a plasma amino acid profile-based index to discriminate between patients with gynecologic cancers and healthy controls. And we tested the diagnostic performance with another data set.

Results: The diagnostic performance was evaluated by using analysis of Receiver Operating Characteristic (ROC) curves. The areas under the ROC curves of the index were 0.92, 0.90, 0.83 for ovarian, endometrial, and cervical cancer, respectively. The sensitivities of the index were 68%, 57%, 52%, and 24% at a specificity of 95% for ovarian, endometrial, cervical cancer, and benign gynecologic disease. Furthermore the sensitivity of the index was significantly higher than that of CA125 for endometrial cancer and comparable to CA125 for ovarian cancer.

Conclusion: This novel index using “AminoIndex Technology” could be potential biomarker in plasma for detection of all the three gynecologic cancers as a novel screening method.
Poster Session I

X-CHROMOSOME-LINKED INHIBITOR OF APOTOSIS (XIAP) IS AN INDEPENDENT POOR PROGNOSTIC FACTOR IN OVARIAN CLEAR CELL CARCINOMA


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Background: X-chromosome-linked inhibitor of apoptosis (XIAP) is one of anti-apoptotic proteins, and confers platinum-resistance. XIAP expression was regulated by HGF/c-Met pathway through Akt in ovarian cancer cells.

Objective: The aim of this study was to investigate the correlation between XIAP and c-Met by immunohistochemistry and compare clinico-pathologic characteristics and survival between high and low expression of XIAP in ovarian clear cell carcinoma (CCC).

Material and methods: Tissue microarrays were made from 90 patients with CCC treated at National Defense Medical College between 1984 and 2007. High expression of XIAP was found in 30(33%) cases and were associated with high expression of c-Met (p< 0.01) and Bcl-xl (p< 0.01). Among 42 cases with stage II-IV CCC, high expression of XIAP was related with lower response rate (8% vs. 60%, p< 0.01), worse progression free survivals (PFS, p=0.02,) and overall survivals (OS, p=0.07). Multivariate analysis showed that expression of XIAP was identified as independent poor prognostic factors of PFS and OS in addition to residual tumors.

Conclusion: XIAP expression was closely related with platinum-resistance in CCC, leading to poor PFS and OS. It was suggested XIAP can be a candidate for new therapeutic target in CCC.
Poster Session I

SYMPTOMATIC LYMPHOCELE AFTER CYTOREDUCTIVE SURGERY IN OVARIAN CANCER: FREQUENCY, RISK FACTORS AND IMPACT ON SURVIVAL


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Introduction: We describe the incidence, impact on survival and the risk factors for symptomatic lymphoceles in ovarian cancer after cytoreductive surgery.

Methods: A retrospective study of ovarian cancer with complete cytoreductive surgery and para-aortic and pelvic lymphadenectomy performed in our institute from 2005 to 2011. Patients were classified into two groups: the symptomatic lymphocele and the control groups.

Results: During the study period, 194 patients with epithelial ovarian cancer underwent cytoreductive surgery and a lymphadenectomy without macroscopic residual disease. Fifty-four patients had symptomatic lymphoceles (28%). In the multivariate analysis, only supra-radical surgery was significantly and independently associated with the risk of symptomatic lymphoceles occurring postoperatively. Median follow-up was 24.8 months [1-74]. Survival rates were not significantly different between the symptomatic lymphocele group and the control group. Two-year disease-free survival was 54% for the lymphocele group and 48% for the control group. Two-year overall survival was 90% for the lymphocele group and 88% for the control group.

Conclusions: Symptomatic lymphoceles occur frequently after cytoreductive surgery in ovarian cancer. Supra-radical surgery is an independent risk factor. The occurrence of symptomatic lymphoceles does not decrease survival. Nevertheless further studies are needed to reduce the risk of lymphoceles in such patients.
Poster Session I

PROGNOSTIC FACTORS AFTER CONSERVATIVE TREATMENT OF “STAGE I” SEROUS BORDERLINE OVARIAN TUMOR: RESULTS OF A LARGE SERIES OF 119 CASES

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Objectives: The aim of this study was to evaluate the prognostic factors of recurrence after conservative treatment of a large series of “apparent” stage I serous borderline ovarian tumors (SBOT).

Methods: A review of 119 patients treated conservatively between 2000 and 2010 with data on the follow-up. All pathological slides were reviewed by the same expert pathologist. Prognostic factors of recurrences were studied (age, histologic subtypes, surgical procedures...).

Results: Conservative procedures were: unilateral cystectomy/UC (n=43; 36%); unilateral salpingo-oophorectomy/USO (n=50; 42%); bilateral cystectomies (n=11; 9%) and USO+CC (n=15; 13%). Twenty-one (18%) & 13 (11%) had stromal microinvasion and/or micropapillary pattern. With a median follow-up of 45 months, 40 (33%) patients recurred (in whom 10 had peritoneal recurrence during the 1st recurrence). Two of these patients had evolution in the form of invasive recurrence. None patient died of disease. Only 2 prognostic factors of recurrence were identified in multivariate analysis: the young age of the patients (< 30 years old) & the bilaterality of the tumours (n=26).

Conclusions: In this series (representing the largest series reported of conservative management of stage I SBOT), the risk of recurrence is not related to the histologic subtypes of the tumor (micropapillary, stromal microinvasion) nor to the surgical conservative procedures used. The rate of invasive recurrence is very rare in this context. Young age and bilaterality of the tumors are risk factors of recurrence suggesting that management of the fertility preservation (before potential recurrence) should be improved in this subgroup.
Poster Session I

OUTCOMES AFTER CONSERVATIVE SURGERY FOR OVARIAN BORDERLINE RECURRENCE AFTER CONSERVATIVE MANAGEMENT OF STAGE I SEROUS BORDERLINE OVARIAN TUMOR

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Objectives: The aim of this study was to evaluate the impact of conservative management of recurrence after conservative treatment of stage I serous borderline ovarian tumors (SBOT).

Methods: Patients with a stage I serous LMPOT treated conservatively between 2000 and 2010 were retrospectively reviewed with data on the follow-up. All pathological slides of initial tumor or relapse were reviewed by the same expert pathologist.

Results: 119 patients were reviewed, forty patients had relapsed and none died from ovarian disease. 26 patients had conservative procedures for borderline recurrence. The conservative procedures for the first relapse were: unilateral cystectomy/UC (n=12); unilateral salpingo-oophorectomy/USO (n=10); bilateral cystectomy (n=1) and USO+CC (n=2) and one patient had a salpingectomy. 19 patients had only 1 conservative surgery for recurrence, 4 had two conservative surgery and 3 patients had 3 conservative managements for relapse. We obtained 11 pregnancies after conservative management of ovarian relapse. 10 (40%) patients recurred after conservative management of ovarian recurrence, in whom 5 had peritoneal recurrence under the form of noninvasive implants. Two of these peritoneal recurrent patients had evolution in the form of invasive recurrence (1 invasive implant and 1 ovarian adenocarcinoma) respectively after the 2nd and 3 relapse. None patient died from disease.

Conclusions: In this series, the conservative management of ovarian recurrence of stage 1 SBOT appeared to be a safe and useful procedure. Nerverless considering the high rate of successive relapse and the risk of invasive recurrence, an oophorectomy should be discussed after achievement of the parental project in patients having a recurrence.
Poster Session I

WHAT IS THE ROLE OF CA125 ASSAY IN PREDICTION THE MALIGNANT NATURE OF AN ADNEXAL MASS

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Introduction: Ovarian cancer is a leading cause of Gynecologic cancer death among women.

Objective: Dertermine the role of CA$_{125}$ in detection of malignant nature of an adnexal mass.

Methods: This is a descriptive inferential study. 100 women with ovarian masses were selected. All women were submitted to serum determination of CA$_{125}$. The data were analyzed by SPSS-13 software.

Results: The concentration of CA$_{125}$ in serum of patients with ovarian cancer was significantly higher than that in patients with Benign tumors (714±486 vs 134±167) p=0.001.

Conclusion: These data confirm that CA$_{125}$ is the important marker in the diagnosis of ovarian cancer.
Poster Session I

MAGNETIC RESONANCE IMAGING FINDINGS OF GRANULOSA CELL TUMOR OF THE OVARY

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Background and aims: Granulosa cell tumor (GCT) of the ovary is unusual ovarian malignancy that may present with signs and symptoms related to estradiol secretion. Preoperative diagnosis of GCT is clinically important. The aims of this study were to clarify the magnetic resonance imaging (MRI) findings of GCT.

Methods: Between 2005 and 2010, six patients diagnosed pathologically with GCT. All tumors were adult type. We retrospectively assessed the MRI and clinical findings of GCT patients.

Results: The mean age of patients was 62.0 years (range, 37 to 82 years). All but one patient were postmenopausal. Four patients presented with abnormal uterine bleeding, one with secondary amenorrhea, and the remaining one with incidentally. All tumors were unilateral. The mean size of tumors was 7.2 cm in diameter (range, 2.9 to 10.1 cm). In five tumors, MRI revealed solid adnexal masses with variable amount of cystic components. Remaining one was entirely cystic. In four tumors, high signal intensity was identified on fat-saturated T1-weighted image in the tumor, which was considered as a hemorrhagic content. The mean uterine endometrial thickness was 5.0 mm (range, 2.6 to 13 mm).

Conclusions: Hemorrhage in the tumor, accompanied with uterine change may be a clue in MRI diagnosis of GCT.
Poster Session I

NEOADJUVANT CHEMOTHERAPY IN ADVANCED EPITHELIAL OVARIAN CANCER

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Background: This study was performed to determine the different outcome and contributing factors in women with advanced epithelial ovarian cancer in patients after primary debulking surgery (PDS) versus interval debulking surgery (IDS).

Methods and material: In this retrospective cohort study, 179 consecutive patients with stage 3 or 4 of ovarian cancer attending to a tertiary center in Tehran, Iran since 2003 to 2009 were recruited. 144 patients underwent primary PDS, and 35 patients were treated with median of 4 cycles of platinum-taxane-based chemotherapy and then underwent IDS. Overall survival and progression free survival (PFS) calculated by Kaplan-Meier curves. Univariate and COX regression analysis were performed to evaluate the surgical outcome and contributing factors in IDS.

Results: 144 patients (81%) were treated with primary cytoreductive surgery and 6 cycles of platinum-taxane chemotherapy and 35 (19%) underwent IDS after neoadjuvant chemotherapy (NACT), there were 14 (40%) partial response and 19 (54%) stable disease and 2 (5%) progressive disease after NACT. Optimal cytoreductive surgery were achieved in 85% of patients underwent IDS compared with 58% in PDS (p=0.02) operative complications such as blood transfusion, fever, organ damage, and hospital stay were significantly higher for PDS.

In neoadjuvant chemotherapy among predictive factors for optimal surgery such as histology, size of tumor, CA125 level, pleural effusion, omental cake, tumor burden which found by imaging, only extensive omental disease and involvement of the mesentery of bowel were found to be predictive.

No significant difference was observed in Progression free survival (PFS) and overall survival (OS) in the 2 groups. PFS (in NACT 18.2±2.4 vs 21 months in PDS p=0.16) and OS 38.8±1.9 vs 41.5 months p=0.66.

Conclusions: According to the obtained results, in patients with advanced epithelial ovarian cancer NACT followed by surgery improved the complications of surgery without impaired survival and in patients with bulky omental cake it is better to remove bulky tumor as a front line of treatment.
Poster Session I

TARGETING ADIPOCYTES BY METFORMIN TO MODULATE OVARIAN CANCER PROMOTING EFFECTS OF ADIPOSE TISSUE

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Background: In epithelial ovarian cancer, factors secreted by adipocytes can promote homing, growth and migration of ovarian cancer cells and thus enhance omental metastasis. These adipocytes also act as fuel depot for meeting the energy needs of fast growing tumor cells.

Objective: To investigate if metformin modulates adipocytes differentiation and secretion of mitogens and consequently limit their role in promoting ovarian tumor growth and migration.

Experimental Approaches: Mouse preadipocyte cells were differentiated in the presence or absence of metformin. Lipid accumulation and AMP-Kinase activation was measured. Conditioned media from undifferentiated and differentiated adipocytes was used to evaluate ID-8 mouse ovarian cancer cell proliferation and migration. Western blots were performed to examine activation of AMP-kinase.

Results: Conditioned media from differentiated but not from undifferentiated adipocytes, increased ID-8 cell migration (p< 0.05) and proliferation by two fold (p< 0.05). These tumor promoting effects were prevented if the adipocytes were pretreated with metformin (p< 0.05). Metformin treatment (2-4mM) inhibited the proliferation of mature adipocytes by approximately 35% (p< 0.05). Furthermore, metformin (2-4mM) resulted in 50-100% inhibition of adipogenesis (p< 0.05) by reducing neutral lipid accumulation. Inhibition of adipogenesis by metformin was accompanied by increase in phosphorylation of AMP-Kinase and Acetyl Co-Carboxylase.

Conclusion: Metformin can inhibit ovarian cancer growth by modulating the environmental milieu around it. It arrests the differentiation and proliferation of adipocytes and inhibits adipocyte mediated ovarian cancer cell proliferation and migration.
Poster Session I

SEROUS TUBAL INTRAEPITHELIAL CARCINOMA PROMOTES EPITHELIAL MESENCHYMAL TRANSITION AND SHOWS A HIGH METASTATIC POTENTIAL

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Objectives: The purpose of this study was to determine the incidence of tubal intraepithelial carcinoma (TIC) in primary ovarian cancer and peritoneal carcinoma, and to explore its molecular characteristics, especially focusing on epithelial mesenchymal transition (EMT).

Method: Following institutional review board approval, we examined the presence of TIC in all ovarian cancer patients who underwent salpingo-oophorectomy, which was performed at the department of gynecologic oncology at Hyogo Cancer Center from 2005 to 2011. Immunohistochemical staining for E-cadherin, CD44 variant9, N-cadherin, vimentin, SLUG, smad, p53, Ki-67, ERα and PgR was performed.

Result: A total of 21 TICs were detected. Strong and diffuse immunoexpression of p53 and Ki-67 were observed in more than 70% of TICs. The immunoprofile correlated with EMT, and we observed negative staining of E-cadherin 14/21 (61.9%) and CD44 variant9 19/21 (90.4%), and positive staining of N-cadherin 10/21 (47.6%) compared with normal fallopian tube epithelium.

Conclusion: TIC shows a high metastatic potential through EMT by down-regulation of E-cadherin and a CD44 variant. These results indicate that serous tubal intraepithelial carcinoma is an early high-grade serous carcinoma characterized by mesenchyme.
Poster Session I

CORRELATION OF GENE EXPRESSION PROFILE WITH HISTOLOGICAL FEATURE IN OVARIAN HIGH-GRADE SEROUS CARCINOMA

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Ovarian high-grade serous carcinoma (HGSOC) is a heterogeneous disease with various morphology. We analyzed correlation between histological features and gene expression profile.

Methods: Expression microarray data of HGSOC from Cancer Genome Atlas (n=584), GSE9891 (n=237) and Kyoto University Hospital (n=30) were combined. HE slides of Kyoto University samples were reviewed.

Results: We defined 4 morphological subtypes with specific tumor microenvironment;

1) well-differentiated, papillary or glandular growth pattern,

2) solid growth pattern,

3) local growth pattern with diffuse infiltration of immune cells, and

4) broadly invasive pattern with prominent desmoplastic reaction.

These subtypes significantly correlated with the 4 clusters identified in the microarray (p< 0.05).

Conclusion: Morphological classification of HGSOC should be described in conducting clinical trials using molecular targeting agents because it is relevant to the molecular features.
META-ANALYSIS OF TALC-DUSTED SANITARY NAPKIN AND OVARIAN CANCER RISK

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Cosmetic talc has been hypothesized to increase the risk of ovarian cancer based on its chemical similarity to asbestos and a significant meta-relative risk of 1.3 associated with perineal talc dusting in 20 studies. Based largely on these results, cosmetic talc was nominated to the National Toxicology Program as a human carcinogen, and classified as a group 2B carcinogen by the International Agency for Research on Cancer (IARC) in 2011. In addition to perineal dusting, there are other sources of potential gynecologic exposure to cosmetic talc including talc-dusted sanitary napkins. We analyzed data from one dozen studies that had quantifiable information on talc-dusted sanitary napkins and the risk of ovarian cancer. Fixed effects and random-effects pooled odds ratios were calculated. Of the 12 studies, a significant increased risk of ovarian cancer was observed in one study. The overall fixed effects odds ratio was 1.15 (95% CI 0.98-1.34). The random effects odds ratio was 1.2 (95% CI 0.94-1.52). The results of this study show that genital perineal talc exposure via sanitary napkins is not associated with ovarian cancer risk.
Poster Session I

PRIMARY INVASIVE MUCINOUS OVARIAN CARCINOMA: IMPORTANCE OF THE EXPANSILE VERSUS INFILTRATIVE TYPE IN PREDICTING RECURRENCE AND LYMPH NODE METASTASES

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Aims: Investigate the role of / the importance of expansile versus infiltrative type of primary invasive intestinal type mucinous ovarian carcinoma (mEOC).

Methods: Retrospective study. Differentiation was defined according to Shimizu-Silverberg and expansile/infiltrative type according to Lee-Scully.

Results: Forty-four mEOC were studied out of 104 patients with mucinous ovarian tumor (excluded: 4 benign, 6 borderline, 3 microinvasive, 22 primary gastrointestinal, 9 endocervical type, 6 anaplastic, 2 mixed, 2 mature teratomas, 6 incomplete data).

Three patients out of 10 with apparently stage I infiltrative, and none of 10 expansile mEOC were upstaged to stage IIIC due to lymph node metastases.

Conclusions: Expansile mEOC is mainly diagnosed at an early stage and is not associated with lymph node metastases. Infiltrative mEOC has a worse prognosis and is associated with lymph node metastases. Degree of differentiation was unreliable in predicting recurrence or lymph node metastases.
Poster Session I

CLINICAL CHARACTERISTICS OF BRAIN METASTASIS FORM OVARIAN CANCER: A STUDY OF 51 CASES

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Objective: The aim of this report is to describe the characteristics, pathologic features, treatments and survival of patients with brain metastasis from ovarian cancer at our single institution.

Methods: Between January, 1989 and April, 2011, a total of 4625 women with ovarian cancer were evaluated at Asan Medical Center. A total of 71 patients were identified using the ICD-10 code for malignant neoplasm of ovary, cross-matched with the medical records for brain metastasis. Patients with other synchronous primary tumor were excluded. The clinical and pathologic characteristics, treatment and outcome of patients with brain metastases from epithelial ovarian carcinoma were analyzed using SPSS 12.0.

Results: The incidence of brain metastasis from ovarian cancer in our population was 1.1% (51/4625). The median survival from the diagnosis of brain metastases was 7 months (range: 0-72). Prior cancer relapse before the diagnosis of brain metastases, and multimodal treatment were related to the duration of survival.

Conclusion: Although the prognosis for patients with brain metastases from epithelial ovarian carcinoma is generally poor, palliative therapy may offer symptomatic relief and improvement in the quality of life on ovarian cancer patients with brain metastasis.
Poster Session I

EVALUATION OF RADIATION THERAPY FOR THE LOCAL RECURRENCE OF EPITHELIAL OVARIAN CARCINOMA

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Background and aims: Chemotherapy is a primary treatment for recurrent ovarian carcinoma, and radiation therapy is generally performed as palliative care in limited cases. On the other hand, there have been some reports stating that radiation therapy was effective for the local recurrence of platinum-resistant ovarian carcinoma. In this study, we performed radiation therapy for 16 patients with local recurrence of epithelial ovarian carcinoma to achieve local control, and evaluated its safety and beneficial effects.

Methods: We examined patient backgrounds, recurrence/radiation sites, beneficial effects, and adverse events in 16 patients with local recurrence of epithelial ovarian carcinoma, who underwent radiation therapy between January 2002 and December 2010 to achieve local control of the recurrent lesion.

Results: The numbers of patients according to each progression stage were as follows: stage I, 2; stage II, 1; stage III, 11; and stage IV, 2. The histologic types were: serous adenocarcinoma (n=11), clear cell adenocarcinoma (n=2), and others (n=3). The progression-free survival (PFS) from radiation therapy initiation was a median of 5.4 months. No severe adverse events occurred, excluding grade-3 anorexia in 1 patient.

Conclusion: The present study involving radiation therapy targeted for local control showed a median PFS of 5.4 months, and no severe adverse events. Radiation therapy for recurrent ovarian carcinoma appears to yield PFS equivalent to that with 1 regimen of second-line chemotherapy, suggesting that such radiation therapy may be useful as a treatment strategy in terms of the extension of survival and improvement of the QOL.
Poster Session I

LAPAROSCOPIC INTERVAL CYTOREDUCTION FOR ADVANCED OVARIAN CANCER - A VIDEO PRESENTATION

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Background, aims and objectives: Advanced laparoscopic surgeries are replacing conventional laparotomies in Gynecological Oncology. We present the video of laparoscopic interval cytoreduction for advanced ovarian cancer.

Methods: Patients are placed in the lithotomy position with legs in the stirrups. Two 10 mm ports one for camera and one working port are placed and three 5 mm ports are placed. After systematic staging, the ovarian tumour cytoreduction, hysterectomy, and omenectomy are done, peritoneectomy, Douglasectomy and adhesiolysis are done if necessary. Specimen is extracted from the vaginal route, or if bulky, removed by enlarging one of the working ports.

Results: Complete cytoreduction for ovarian cancer can be achieved just as in the open surgery. Benefits are smaller incision with lesser morbidity, reduced hospital stay, earlier mobilization, and minimal morbidity if found to be inoperable. Other potential benefits may be early adjuvant chemotherapy.

Conclusion: Laparoscopic interval cytoreduction for advanced ovarian cancer can be done safely with good result. The numbers are very small internationally, but a randomized clinical trial shall establish this procedure. Our video presentation aims to draw focus on this.
THE ROLE OF HYBRID PET/CT TO PREDICT SECONDARY OPTIMAL DE-BULKING IN PATIENTS WITH RECURRENT OVARIAN CANCER

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Purpose: To assess the clinical value of FDG-PET/CT in patients with recurrent ovarian cancer that may benefit from secondary optimal debulking surgery.

Methods: From 2004-2011, 282 patients were evaluated for suspected recurrent ovarian cancer. CT scans were performed on all patients with elevated CA-125 levels and/or clinical symptoms. FDG-PET/CT scans were performed on 42 patients with negative, indeterminate or localized CT scans. Nineteen patients who found to have localized recurrent sites underwent surgery in order to achieve secondary optimal debulking and patients with multifocal recurrent sites were referred for chemotherapy. Surgical outcomes were compared to preoperative FDG-PET/CT findings. The ability of FDG-PET/CT to predict optimal tumor debulking was documented.

Results: 18/19 patients underwent secondary debulking surgery. 16/18 patients had optimal tumor debulking and 2/18 patients had suboptimal tumor debulking. Positive predictive value for optimal debulking was 88.9%. Of the 18 patients who underwent cytoreductive surgery, 8 patients (44.4%) show evidence of disease and 10 (55.5%) patients have no evidence of disease. Of the 17 patients with multifocal FDG-PET/CT findings, who did not undergo secondary surgery, 16 patients show evidence of disease (94.1%) and one patient (5.9%) shows no evidence of disease, average time to follow-up of 41 months (range 6-102 mo.).

Conclusion: Our results extend prior reports on the role of fused FDG-PET/CT in the management of recurrent ovarian cancer by predicting favorable surgical outcomes and optimizing patient treatment, however future studies should aim to investigate its impact on survival.
Poster Session I

DISEASE SPECIFIC OUTCOMES AND TREATMENT PATTERNS IN PATIENTS WITH OVARIAN CANCER WITH METASTATIC SPREAD TO THE CENTRAL NERVOUS SYSTEM

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Objectives: The central nervous system (CNS) is a rare location of initial or recurrent metastatic disease in patients with ovarian, fallopian tube, or primary peritoneal carcinoma. The aim of this study was to examine treatment patterns, prognostic factors, and outcomes of patients with these cancers who had documented central nervous system (CNS) metastases and were treated at a single academic institution. Methods: A retrospective chart review was performed of patients diagnosed with ovarian, fallopian tube, or primary peritoneal carcinoma and developed CNS metastases between 1/1/1990 and 7/1/2010 and were treated at our institution. Data collected included demographic and clinical pathologic information, survival, and treatments.

Results: Twenty-three patients were identified with a mean age at diagnosis of 52. The mean time to diagnosis of central nervous system metastases from the time of original diagnosis was 32(0-360) months. The mean time to diagnosis of any recurrence in this patient population was 15.6 months. The majority of patients (70%) did not recur in the CNS first. Seventeen patients were treated with a combination of whole brain radiation and chemotherapy, four patients were treated with stereotactic radiation and chemotherapy and two patients with craniotomy and subsequent chemotherapy. The median overall survival (OS) was 58 (3-444) months. Factors influencing overall survival, time to diagnosis of CNS metastases, and progression free survival were platinum sensitivity and optimal cytoreduction.

Conclusions: In contrast to some previous reports, our data suggest that patients with ovarian, fallopian tube, and primary peritoneal cancer with CNS metastases have an overall survival comparable to patients without CNS metastases. The same well established prognostic factors predict outcomes in patients with CNS metastases as in patients without. In our experience, a multi-modal approach to treatment utilizing a combination of radiation and chemotherapy, as opposed to radiation or chemotherapy alone, yields excellent outcomes in these patients.
Poster Session I

SAFETY AND EFFICACY OF LAPAROSCOPIC AND ROBOTIC PRIMARY CYTOREDUCTION FOR ADVANCED STAGE OVARIAN, FALLOPIAN AND PRIMARY PERITONEAL CANCER

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Objectives: The purpose of this study is to evaluate the feasibility of laparoscopic and robotic-assisted cytoreduction for advanced stage ovarian, fallopian or primary peritoneal cancer.

Methods: This is a retrospective analysis of a prospectively maintained database from 7/2008 to 12/2012 of all videolaparoscopic (VALS) or robotic-assisted (RALS) surgery for advanced-stage disease, with the goal of maximum cytoreduction. This report examines VALS and RALS outcomes, including optimal cytoreduction, intraoperative and postoperative complications and outcomes.

Results: During the study period, 25 patients were operated on for presumed advanced-stage ovarian, fallopian or primary peritoneal cancer. 6 patients were excluded; 4 patients had a different primary on frozen/final pathology and 2 patients refused/were not candidates for cytoreduction. Of the 19 patients included, 9 had VALS, 5 had RALS and 5 were converted to laparotomy(LP). Of these 19 patients, 8 received neoadjuvant chemotherapy prior to debulking. These patients previously underwent diagnostic surgery and were not candidates for primary cytoreduction at that time. 8/9 VALS, 5/5 RALS and 3/5 LP were optimally cytoreduced(<1cm residual disease). Mean EBL was 243ml, 190ml, 850ml and OR time was 396min, 416min, 433min in the VALS, RALS, LP groups respectively. There was 1 intraoperative complication in the LP group and 2 postoperative complications requiring 1 reoperation after VALS and 1 after RALS. Median follow up was 11m with 11NED, 5 deaths and 3 alive with disease.

Conclusions: Laparoscopic and robotic-assisted cytoreduction for primary ovarian, fallopian and primary peritoneal cancer is safe and feasible with low complication rates and acceptable outcomes in selected cases.
Poster Session I

COMPLICATION RATES BETWEEN VIDEOLAPAROSCOPIC VERSUS ROBOTIC-ASSISTED LAPAROSCOPY IN MANAGEMENT OF EARLY, ADVANCED AND RECURRENT OVARIAN, FALLOPIAN AND PERITONEAL CANCER

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Objective: To examine the complications of videolaparoscopy(VALS) versus robotic-assisted(RALS) in the evaluation and management of early, advanced and recurrent ovarian, fallopian tube and primary peritoneal cancer.

Methods: This is a prospective cohort IRB approved study from 7/2008 to 2/2012 of all VAL or RALS surgery performed for the management of early, advanced and recurrent ovarian, fallopian tube and primary peritoneal cancer.

Results: Out of 61 surgeries, 12 were performed for early stage and 49 for advanced and/or recurrent disease. Of the 12 surgeries for early stage, 7 were VALS and 5 were RALS. Of those, there was 1(14.3%) complication postoperatively in the VALS group. In the advanced/recurrent group, 33 surgeries were VALS, 10 were RALS and 6 were laparoscopy intentionally converted to laparotomy(LP). There were 4(12%) postoperative complications in the VALS group, 4(40%) in the RALS group and 1(16.7%) in the LP group. There was 1(16.7%) intra-operative complication in the LP group. In the VALS and RALS group, there were two re-operations; one for breakdown of an anastomosis and the other for bowel perforation. Other complications included pelvic hematoma, cuff separation, UTI, atrial fibrillation and delirium in the VALS group, trocar site cellulitis and vaginal fistula in the RALS group and wound infection in the LP group. There was no difference between VALS and RALS in both the early(Fisher exact p=0.6) and late/advanced(p=0.07) groups.

Conclusions: Complication rates are comparable between VALS and RALS in both early and advanced/recurrent disease making VALS and RALS an acceptable approach in selected patients.
Poster Session I

SUSTAINABLE COMPLETE REMISSION IN RECURRENCE YOLK SAC TUMOUR TREATED WITH TANDEM HIGH DOSE CHEMOTHERAPY & AUTOLOGOUS STEM CELL TRANSPLANTATION

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A 21 year old lady diagnosed with Stage 3 ovarian yolk sac tumor underwent primary cytoreductive fertility sparing surgery followed by conventional courses of chemotherapy with platinum based and Etoposide. Her alphafetoprotein (AFP) level normalized for only two months then began to elevate. Recurrence at cul-da-sac was noted after short period of remission and secondary debulking performed followed by four cycles of conventional chemotherapy. Her disease progressed despite courses of treatments. A joint multidiscipline team management with haematologist was commenced following the failure of conventional chemotherapies. After one cycle of priming conventional chemotherapy, two cycles of high dose chemotherapy (Ifosphamide, Cisplatin and Etoposide) ICE regimen followed by autologous stem cell transplantation were given. With this salvage treatment, she remained in longer period of remission and disease free for more than 30 months while maintaining her reproductive function. These approaches appeared to be a district role for salvage treatment in selected cases of patient with ovarian germ cell tumor especially for those who failed primary conventional chemotherapy. More studies on ovarian germ cell tumor treated with HDCT are needed to further define the subset of patient who would benefit with this approach.
Poster Session I

NVP-BEZ235, A DUAL PI3K/ mTOR INHIBITOR, SUPPRESSES TUMORIGENICITY OF OVARIAN CLEAR CELL CARCINOMA CELLS

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Background: Recently, it has been shown that ovarian clear cell carcinoma (CCC) has a high frequency of activating PIK3CA mutations. NVP-BEZ235 (BEZ235) is a dual PI3K/ mTOR inhibitor and inhibits both mTORC1 and mTORC2.

Objective: The purpose of the current study was to determine whether BEZ235 suppresses tumorigenicity of CCC.

Material and methods: We used eight CCC cell lines and five serous adenocarcinoma (SAC) cell lines. IC50 to BEZ235 or mTOR inhibitor, Temsirolimus was determined by WST-8 assay. The expressions of PI3K-Akt-mTOR signaling proteins were examined by western blotting. Cell cycle distribution was analyzed by flow cytometry. Apoptotic cells were counted by Annexin V staining. We also investigated the effects of BEZ235 on tumor growth in a nude mice xenograft model. Mice bearing subcutaneous tumors of OVISE or TU-OC-1 received 3 weeks of treatment with vehicle or BEZ235 (25 or 50 mg/kg/day). Tumor volume was measured twice weekly.

Results: The IC50 to BEZ235 for CCC cell lines were lower than for SAC cell lines. The IC50 to Temsirolimus were higher than BEZ235 in CCC cell lines. pAkt expression in CCC cells was suppressed after exposure to BEZ235 but not Temsirolimus. CCC cells exhibited G1 cell cycle arrest after being exposed to 10 or 100 nM BEZ235, and apoptotic cells were induced by higher concentrations of the agent. Treatment of mice bearing OVISE or TU-OC-1 with BEZ235 significantly suppressed tumor growth without severe weight loss.

Conclusion: These results suggested that BEZ235 is worth exploring as a therapeutic agent for CCC.
Poster Session I

DEVELOPING A NEW COMPREHENSIVE PSYCHOSOCIAL CARE PROGRAM SPECIFICALLY TAILORED FOR GYNECOLOGICAL ONCOLOGY PATIENTS AND THEIR FAMILIES

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Ireland currently has no access to an established psycho oncology service outside of the capital city, Dublin. Patients who attend their gynecologist or oncologist for treatment outside of Dublin depend on voluntary organizations for their therapeutic support. These services work outside of the National Health Service, and have major limitations on what they can offer.

Gynecological cancers have a direct impact on the lives of thousands of Irish women and their families. Annually this number is increasing. It has been well documented internationally that cancer patients who receive the appropriate emotional support are less likely to attend the hospital, feel psychologically stronger, higher compliance rate to treatment and thus increasing survival (Carlson, Bultz, 2002, 2003, 2004). A. Mitchell (2011) highlights the importance of a psychosocial intervention in directly improving anxiety, depression and quality of life in women with gynaecological cancer.

We describe the establishment of a comprehensive psycho oncology service in the southern part of the country but unique to Ireland. It specifically meets the needs of gynaecological oncology patients, their families and significant others. We discuss the sourcing of therapists from a broad therapeutic background (systemic psychotherapists, psychologists, psychotherapist, psycho-sexual therapist, child psychologist, art therapists and play therapists). We explain the geographic challenges in meeting the patients’ needs group.

We outline a specific training module facilitated by clinicians from an interdisciplinary background addressing clinical, practical and emotional needs of this patient group. We examine the need for protocols and the logistics for those embarking on a similar journey.
Poster Session I

STAGE IV OVARIAN CANCER: PUTTING YOUR MONEY WHERE YOUR MOUTH IS!

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In the United States in 2007,* 80,976 women were told that they had a gynaecological cancer, and 27,739 died from a gynaecological cancer. Currently Ireland does not have a comparative national data base but it would not be unreasonable to directly compare the two countries. In doing so it translates as one in 3.3 women that are seen by a gynecologist will eventually die from the disease.

With the use of video extracts the author will draw on an interview from one of her clients, Jane a 28 year old accountant who has stage four ovarian diagnosis. Communication for professionals working in cancer is complex due to the different sites, stages, causes, screening strategies, treatment strategies and responses to treatment. Cancer information is emotionally charged due to the serious and life threatening nature of the disease. According to Bultz and Carlson 2003 poor communication can be attributed to some of the emotional distress that half of all cancer patients experience. Possibly one of the more challenging aspects to communication within cancer is the patients and the doctors response-their psychological positioning and socio-emotional status.

The systemic effect of a cancer diagnosis reaches far beyond the realms of those patients and their significant other(s) that sit before the gynecologist as he or she tells the bad news. The importance of this events and all those meeting and conversations that take place subsequently have a profound effect on the individuals ability to cope.

We emphasize the lack of psychosocial support for this patient group.
Poster Session I

CHARACTERISTICS AND OUTCOME OF BORDERLINE OVARIAN TUMOR IN KING CHULALONGKORN MEMORIAL HOSPITAL

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Borderline ovarian tumor (BOT) is a distinct diagnosis which comprised 5-15% of epithelial ovarian tumor. From observation, BOT in our institute was more common in mucinous cell type which was different from other reviews. This study was conducted to evaluate characteristic, treatment outcome and recurrence of BOTs in our institute.

Retrospective review the chart of BOT patients was performed to conclude all data. From the year 2006 to 2010, all 55 cases of BOT were reviewed in the aspect of general characteristic, presenting symptoms, tumor marker, pathologic diagnosis, operation and outcome included recurrence.

From 55 cases of BOTS, mean age of patients was 42 years old (range 13-89 years old). The presenting symptoms were palpable mass, abdominal discomfort and pelvic pain, respectively. One fourth of the patients had no symptom. Most common cell type was mucinous (72.7%). Serous cell type was found 21.8% of cases. Common procedures were Salpingo-oophorectomy, TAH-BSO and TAH-BSO with lymph node sampling, respectively. Median follow up time is 38 months (range 14-71 months). Recurrence was found 5 cases from total 55 BOTs cases. Common recurrence was arising from serous cell type and the patient who had residual tumor in primary operation. Higher stage was associated with higher incidence of recurrence.

In conclusion, our institute, mucinous borderline is the most common cell type. In the aspect of recurrence, the results were similar to other studies. The optimal treatment of recurrence was controversy and need for further information.
Poster Session I

NO ASSOCIATION BETWEEN THE CYP1B1 VAL432LEU POLYMORPHISM AND OVARIAN CANCER RISK: A META-ANALYSIS

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Introduction: The aetiology of ovarian cancer remains unclear. Polymorphisms within genes responsible for oestrogen metabolism may influence the risk of developing ovarian cancer. CYP1B1 enzyme catalyzes the formation of genotoxic 4-hydroxyoestradiol (4-OH E2), and CYP1B1 V432L polymorphism could modify an individual's risk of ovarian cancer. There are only a limited number of studies, which explore the association between CYP1B1 polymorphisms and ovarian cancer risk.

Methods: Papers were identified using online databases. Data on genotype frequencies was collected. Case-control studies published up to 1st April 2012 were included. We used fixed/random effect models to estimate pooled odds ratios (OR) with 95% confidence intervals. Chi-square based Q-test was used to test for heterogeneity.

Results: No difference in frequency distribution of V432L V/V genotype (wild-type) was observed in pooled results of 5 included studies. The difference in variant genotype (V/L and L/L) frequencies for ovarian cancer was not associated with increased risk with pooled OR: 1.14; 95% CI: 0.91-1.42 and 1.15 (0.89-1.23) respectively.

Conclusions: In a pooled analysis of CYP1B1 V432L polymorphisms and ovarian cancer risk, there is no overall association between variant genotypes and risk modification. The meta-analysis included only 5 studies, and more studies are required to address such an association.
**Poster Session I**

**LENGTH OF STAY FOLLOWING OVARIAN CANCER SURGERY: DOES STAGE MATTER?**


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**Introduction:** Inpatient hospital care remains a major expense in the treatment of patients with ovarian cancer, despite significant advances in treatment. Reducing post-operative length of stay (LOS) has the potential to decrease healthcare costs, risk of hospital-acquired events and to improve patient's quality of life.

**Aim:** To determine if age of patient, FIGO stage and treatment group influence LOS.

**Method:** Retrospective review of 54 case notes randomly selected from patients who underwent surgery for ovarian cancer in a 2-year period (January 2009-2011). Data was collected on FIGO stage, treatment group, LOS and patient demographics. Results were statistically analysed using Mann Whitney test.

**Results:** Median post-operative LOS was 7 days (IQR 6-9). Median LOS for stage 1 ovarian cancer patients was 6 days (IQR 5-8) versus 7 days (IQR 6-9) for patients with stage 2-4 disease (p=0.08). There was no difference between the LOS in stage 2-4 patients who underwent primary surgery and interval debulking surgery (IDS) (median 7 days versus 7.5). Similarly, LOS was also independent of patient age (< 60 yrs versus >61 yrs, p >0.05).

![Length of stay following ovarian cancer surgery](image-url)

**LOS versus stage of ovarian cancer**
Conclusion: Stage of disease does not appear to increase LOS following ovarian cancer surgery. Our median LOS is greater than the national average of 5.5 days therefore we have implemented an enhanced recovery pathway with the aim to reduce inpatient stay and facilitate the provision of cost-effective care.
INCIDENCE OF SEROUS TUBAL INTRAEPITHELIAL NEOPLASIA IN IRISH WOMEN WITH BRCA MUTATIONS UNDERGOING RISK REDUCING SURGERY

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Epithelial ovarian cancer is the fourth most common cancer in Irish women. Previous studies have shown that 2.3% to 17% of patients will have occult carcinoma diagnosed at the time of prophylactic surgery. The fimbria of the fallopian tube has become a focus of interest in the last decade as the most common site of origin of occult disease.

This is a study utilising archived tissue samples from women who have had bilateral salpingo-oophorectomy for risk reducing surgery due to BRCA mutations. Patients were recruited from the Mater Misericordiae University Hospital and the Mater Private Hospital in Dublin, Ireland.

A total of 24 women with BRCA mutations or variants underwent prophylactic surgery between January 2005 and May 2011. The median age of the patients was 47.3 years (range 34 to 64 years). 18 of the 24 women (75%) had the procedure done laparoscopically and 14 women (58.3%) also had a hysterectomy as part of their risk reducing surgery. Five patients (20.8%) had serous tubal intraepithelial neoplasia (STIN) confirmed on histology following surgery.

Archived tissue samples of fallopian tubes and ovaries from the remaining 18 patients were used for further pathological analysis.

Step sectioning and Immunohistochemical assessment namely p53 protein mutation analysis, MIB1 analysis (a proliferative marker) and \(\gamma\)-H2AX analysis (localizes areas of DNA damage) was performed on all specimens to identify serous tubal intraepithelial neoplasia (STIN).

Our study provides information on the incidence of STIN in BRCA positive Irish women and helps us counsel future patients more appropriately.
Poster Session I

CLINICAL PRESENTATION AND MANAGEMENT OF MALIGNANT GERM CELL OVARIAN TUMOURS IN BPKOIRALA MEMORIAL CANCER HOSPITAL

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Background: Germ cell malignancies account for about 5% of all ovarian cancers. Commonly seen in young females, germ cell malignancies are highly chemosensitive and are potentially curable with surgery and chemotherapy. This study is the first of its kind regarding the epidemiology, management and outcome of patients with malignant germ cell tumour in Nepal.

Objective: To analyze the clinical presentation and management outcomes of malignant germ cell tumours managed in B.P. Koirala Memorial Cancer Hospital, Nepal.

Methodology: Descriptive study. Case records of GTD patients attending B.P. Koirala Memorial Cancer Hospital from January 1999 to December 2009 were analyzed regarding their illness history, clinical examination, investigations, treatment, follow-up and outcomes measured.

Observations: Total 65 cases of malignant germ cell tumours, aged 2 to 58 years (mean 21.7 years) were received. 42% cases were Tibeto-Burmese; 30% were Indo-Aryans. There were 15 cases (23%) of dysgeminoma, 21 endodermal sinus tumor (32%), 16 Immature Cystic Teratoma (24.5%), 9 (14%) Mixed Germ Cell, 2 unclassified GCT (3.5%) and 2 malignant transformation in teratoma (3.5%). 33 (49.5%) patients had early stage disease, 37 (57%) underwent fertility preserving surgery. 4 cases (9%) due to disseminated disease, underwent neoadjuvant chemotherapy followed by debulking surgery. 51 cases (78.5%) received adjuvant chemotherapy (BEP or EP regimen). The overall survival was 70%.

Conclusion: Early stage germ cell malignancies can be safely managed by fertility preserving surgery followed by, chemotherapy if indicated. For advanced diseases, neoadjuvant chemotherapy followed by surgery can be undertaken with curable intent.
**Poster Session I**

**PROPER INDICATIONS FOR FERTILITY-SPARING SURGERY IN YOUNG PATIENTS WITH EARLY STAGE EPITHELIAL OVARIAN CANCER**


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**Objectives:** To evaluate the safety of fertility-sparing surgery (FSS) in young patients (≤ 40 years) with stage I epithelial ovarian cancer by comparing with radical surgery (RS).

**Methods:** Of 239 Patients with stage I EOC, 134 underwent FSS and 105 underwent RS. Patients were categorized into four disease categories (stage IA and grade 1 or 2; stage IA and grade 3; stage IC and grade 1 or 2; and stage IC and grade 3).

**Results:** There were no significant differences in clinicopathologic characteristics between RS and FSS groups in each disease categories. There were no differences in 5-year DFS (82% vs. 80%, P=0.805) and OS (86% vs. 89%, P=0.514) between RS and FSS groups. The 5-year DFS for RS and FSS groups were 91% and 89% (P=0.777) for stage IA, grade 1-2 disease, 87% and 83% (P=0.770) for stage IA, grade 3 disease, 69% vs. 71% (P=0.709) for stage IC, grade 1-2 disease, and 72% and 70% (P=0.565) for stage IC, grade 3 disease. The 5-year OS for RS and FSS groups were 97% and 97% (P=0.951) for stage IA, grade 1-2 disease, 94% and 89% (0.853) for stage IA, grade 3 disease, 73% and 76% (P=0.870) for stage IC, grade 1-2 disease, and 77% and 81% (P=0.641) for stage IC, grade 3 disease.

**Conclusion:** Fertility-sparing surgery can be performed without compromise of disease-free and overall survival in young patients with stage I epithelial ovarian cancer regardless of sub-stage and grade of disease.
Poster Session I

THE EFFECT OF ENDOSTATIN MEDIATED BY HUMAN MESENCHYMAL STEM CELLS ON OVARIAN CANCER CELLS IN VITRO

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Introduction: Endostatin is the most potent inhibitor of tumor angiogenesis. However, endostatin protein has a short half-time and virus-mediated endostatin gene therapy has serious toxicity, which limits the application of endostatin in clinical therapy. Mesenchymal stem cells (MSCs) are considered to be able to accumulate at the site of cancers with high specificity and may be used as a new delivery of endostatin.

Materials and methods: The MSCs from the human bone marrow were transfected with recombinant adenovirus encoding endostatin and EGFP (MSC-EN cells). The tropism capacity of MSCs was quantitatively assayed in vitro using the Millicell system. To investigate the impact of secreted endostatin on cancer cells, SKOV3 cells were cocultured with MSC-EN cells in Millicell for 48h, then apoptosis and cell cycle were analyzed on a flow cytometer.

Results: In contrast with 293 cells and saline, SKOV3 cells significantly stimulated migration of MSCs, the number reached 919.67± 19.96 (P < 0.05). The endostatin produced by MSC-EN cells made 13.08 ± 0.21% SKOV3 cells undergo early stage apoptosis (control 3.23 ± 0.73%, P < 0.05) and 82.05 ± 2.65% SKOV3 cells accumulate in the G0/G1 phase (control 66.51 ± 2.91%, P < 0.05).

Conclusion: We found that MSCs possessed great migratory capacity in vitro and the human ovarian adenocarcinoma cell line SKOV3 could significantly induce the migration of MSCs. Our results provided evidence that MSCs could be utilized as a powerful delivery system of endostatin. The endostatin produced by MSC-EN cells could inhibit the proliferation of SKOV3 cells.
Poster Session I

ROLE OF THE LAPAROSCOPIC RE-STAGING FOR GRANULOSA CELL TUMOR OF THE OVARY

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To evaluate the role of laparoscopic staging in patients with incompletely surgically staged ovarian granulosa cell tumor (OGCT).

All medical records of patients with OGCT that were managed as inpatients from 1970 to 2011 were reviewed.

We found from our database a total of 283 patients with a median age of 44 years (range 4-82 years). Two-hundred forty-three (86%) patients had adult type and 39 (14%) had juvenile granulosa cell tumors. One hundred forty women (49%) received standard primary surgical staging that included a hysterectomy, whereas 142 (51%) underwent conservative surgical treatment. Among the latter group, 71 were incompletely surgically staged at another institution. We completed the surgical management with laparoscopic peritoneal assessment, infracolonic omentectomy and abdominal/pelvic washings after a delay mean time from the diagnosis of 3.5 months (range 1-8.8 months). The mean hospital stay was 2.7 days (ranged 1-6). The initial clinical International Federation of Gynecology and Obstetrics (FIGO) stage of this group was IA in 40 patients, IC in 25, IIIB in 4, IIIC in 2. After second surgery performed by laparoscopy, among the IA patient's group, 1 was upstaged to IIA and 3 to IIB stage and respectively patients with IC stage, 1 was upstaged to IIIC and 1 to IIB. Adjuvant chemotherapy was given to the upstaged patients.

Our series demonstrated that laparoscopy is feasible and efficient to perform a correct staging of patients who were previously incorrectly staged for OGCT. Surgical restaging seems to have a role in the management of OGCT.
**Poster Session I**

**THE BMP SIGNALING PATHWAY LEADS TO ENHANCED PROLIFERATION IN SEROUS OVARIAN CANCER-A POTENTIAL THERAPEUTIC TARGET**

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**Background and aims:** Members of the transforming growth factor-β (TGF-β) superfamily transduce signals via SMAD proteins. SMAD2 and SMAD3 mediate TGF-β signaling, whereas SMAD1 and SMAD5 transduce bone morphogenetic protein (BMP) signals. We would like to identify the function of BMP/SMAD5 signaling in serous ovarian cancer.

**Methods:** The expression of SMAD5 and phosphorylated SMAD5 (pSMAD5) protein were investigated by immunohistochemical analysis using clinical samples of serous ovarian cancer. Following treatment with recombinant BMP2 (rBMP2) and dorsomorphin (DM) separately, western blotting was performed to observe the cytoplasm and the nucleus of pSMAD5 protein separately; cell proliferations detected by WST-1 assay and flow cytometric analysis in SK-OV-3 and IOSE cell line. The impact of DM or rBMP2 on tumor growth was observed in a mouse model of serous ovarian cancer.

**Results:** Inverse correlation observed between pSMAD5 expression in nucleus and the prognosis of patients with serous ovarian cancer. Treatment of SK-OV-3 with rBMP2 stimulated pSMAD5 translocation cell percentage, and the effects were inhibited by DM. *In vitro* and *in vivo* experiments, clearly demonstrated BMP2 stimulated proliferation of serous ovarian cancer and this effect was inhibited by DM.

**Conclusions:** Our data suggests BMP/SMAD5 signaling play an important role and is promising as a potential therapeutic target in serous ovarian cancer.
Poster Session I

COMPARATIVE STUDY OF SERUM LINE-1 METHYLATION LEVEL IN OVARIAN CANCER PATIENTS AND CONTROLS

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Material and method: LINE-1 methylation statuses were examined by Combined Bisulfite Restriction Analysis method from serum of 20 Epithelial Ovarian Cancer patients and 20 Controls who were admitted in Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University between September 1st, 2011 and December 31st, 2011.

Results: The LINE-1 methylation level and patterns of the Epithelial Ovarian Cancer patients were compared to the controls. Only % ⁶⁶C⁶⁶C (unmethylation) was observed to be significantly different (34.30% ± 2.07 and 30.73% ± 6.95 in cancer and control group, p = 0.002). The overall methylation level (41.62% ± 2.71 and 42.52% ± 4.76 in cancer and control group, p = 0.158) and other methylation patterns were not significantly different between cancer and control group.

Conclusion: This study has demonstrated that % ⁶⁶C⁶⁶C of LINE1 methylation in serum of the ovarian cancer patients was significant higher than the controls. The prognostic influence and the application for more benefit should be evaluated in further studies.
Poster Session I

HUMAN EPIDIDYMIS PROTEIN 4 (HE4) AS A BIOMARKER IN PATIENTS WITH OVARIAN CANCER IN THE POPULATION OF CZECH WOMEN

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Aim: The incidence of ovarian cancer in the Czech Republic is around 23 per 100000 women per year. The aim of this study was to evaluate biomarkers that might increase the sensitivity and specificity of CA125, which is routinely used in diagnosis of ovarian cancer, and to verify the results on the population of Czech women.

Methods: Serum was obtained from 553 women with ovarian tumors - EOC stage I - IV and with benign ovarian neoplasms. The samples were analyzed for levels of CA125, HE4, TK, TPS and Monototal, and were compared to clinical status. In all cases ROMA index was calculated and FSH was used to determine exact menopausal status. Logistic regression models were estimated for all markers and their combinations, with cross-validation analysis performed to obtain the sensitivities and specificities at 95%.

Results: ROC-AUC, sensitivity and negative predictive value in all our comparison groups, for monitored markers or their combinations related to age or FSH, was always greatest for ROMA2, followed by CA125, ROMA1 and HE4. Mean values for all markers were significantly different between patients with benign masses and a cancer.

Conclusions: The sensitivity of HE4 for diagnosis of ovarian cancer is high, but combined with CA 125 in ROMA index it was found to be more accurate predictor of malignancy than either marker alone. This is especially true in the cohort of postmenopausal women. Reliability of ROMA index increased with the concurrent routine FSH assessment in order to differentiate the pre- and postmenopausal status.
Poster Session I

STUDY ON THE MECHANISM OF TWEAK RESTORING CISPLATIN SENSITIVITY BY REGULATING AUTOPHAGY AND APOPTOSIS IN EPITHELIAL OVARIAN CANCER

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Background: Resistance to cisplatin-based therapy is a major hurdle to successful long-term treatment of human epithelial ovarian cancer (EOC). Tumor necrosis factor (TNF)-like weak inducer of apoptosis (TWEAK) is a multifunctional cytokine that regulates cellular proliferation, metastasis, and apoptosis. However, the effect of TWEAK on cisplatin resistance in epithelial ovarian cancer (EOC) remains elusive.

Objective: Study the effect of TWEAK on cisplatin resistance, and investigate the detail mechanism of TWEAK restoring cisplatin sensitivity.

Methods: The proliferation of cisplatin resistant human EOC cell line A2780/CDDP and its parental cell A2780 was determined using CCK-8 assay. Migration rates were measured by wound healing assay. The expression of autophagy-associated proteins LC3II and Beclin 1 was detected by western blot, and cell apoptosis was detected by FCM in those two cell lines. The phosphorylation of ERK1/2 and AKT was determined by Western blot in A2780/DDP cells.

Results: TWEAK had no effect on cell migration, while it significantly down-regulated the ability of cell proliferation in A2780/CDDP cells (p< 0.05). Compared with A2780 cells, the protein expression of LC3II and Beclin 1 was increased in A2780/CDDP cells. TWEAK further up-regulated the protein expression of LC3II and Beclin 1, and promoted apoptosis in A2780/CDDP cells. Moreover, TWEAK inhibited the phosphorylation of ERK1/2 and AKT in A2780/CDDP cells.

Conclusion: Our study first demonstrated that TWEAK might restore cisplatin sensitivity by excessively activating autophagy, promoting apoptosis and down-regulating ERK1/2 and AKT pathway in A2780/CDDP. Our results provide theoretical basis for developing new therapy for cisplatin chemoresistance in EOC.
Poster Session I

MANAGEMENT OF OVARIAN TUMORS OF VARYING MALIGNANT POTENTIAL DURING PREGNANCY

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Introduction: Ovarian tumours are found in 1:1000 pregnancies and only 3-6% are malignant. Here, we report 4 cases of tumors of varying malignant potential diagnosed and managed during pregnancy.

Case reports: In two cases, primigravidas were diagnosed with a cystic ovarian mass with solid areas on ultrasound, one when she presented with sudden onset abdominal pain at 9 weeks, the other incidentally at 16 weeks’ gestation. Serum CA-125 was 209U/ml and 4.92U/ml respectively. They underwent staging laparotomy and unilateral salpingo-oophorectomy at 14 weeks’ and 18 weeks’ gestation respectively. Histopathology of both was serous-cystadenofibroma. Both had an uneventful pregnancy, successful vaginal delivery at term and have no evidence of disease.

Case 3, G2P1+0+0+1 presented at 31 weeks’ gestation with acute pain abdomen. Ultrasound diagnosis was ovarian cyst with rupture. She underwent emergency laparotomy, cesarean section, left salpingo-oophorectomy and omentectomy. Histopathology showed borderline mucinous cysadenocarcinoma. At 3 years follow-up she has no evidence of disease.

Case 4, G2P1+0+0+1 was diagnosed incidentally at 22 weeks’ gestation with a stage IV malignant germ cell tumor with liver parenchymal lesion on MRI. She received three cycles of neoadjuvant chemotherapy (BEP regimen). At 35 weeks she underwent emergency cesarean-hysterectomy, bilateral salpingo-oophorectomy and omentectomy for poor biophysical profile and delivered 1630g male baby. Postoperatively she received two cycles of chemotherapy. Both mother and baby are doing well.

Conclusion: Although most ovarian tumors in pregnancy are benign, malignancy should be kept in mind and treatment individualized. Chemotherapy is an option in women who wish to continue pregnancy.
Objective: To evaluate the clinical features, diagnosis and outcome of borderline ovarian tumours.

Methods: In this retrospective analysis, case records of 14 patients with diagnosis of borderline ovarian carcinoma, between 2008 to 2011 were analysed.

Results: The median age was 32 years (range 15 to 58 years). Presenting symptoms included acute abdominal pain (50%), mass per abdomen (28.6%) and postmenopausal bleeding (7.1%). Ultrasound findings were complex cystic mass (57.1%), simple ovarian cysts (28.6%) or multiloculated cyst (14.3%). Serum CA-125 was elevated in only 5 (35.7%) patients, with levels between 19.5-137 U/mL. Risk of malignancy index (RMI) was >200 in only four (28.6%) cases. Six (42.8%) underwent upfront complete surgery, i.e., staging laparotomy, peritoneal cytology, total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy. Eight had conservative surgery - unilateral salpingo-oophorectomy in 4 cases and combined with ovarian cystectomy of the opposite ovary in 4 cases. Of them, 2 underwent complete surgery after final histopathological diagnosis. Most cases were in stage Ia (57%). Final histopathological diagnosis was serous in nine (64.2%) and mucinous in 5 (35.7%). Two patients received postoperative chemotherapy with carboplatin and paclitaxel one due to microinvasive histopathology and other due to cytology positive for malignant cells. All the patients are on regular follow up with no evidence of disease.

Conclusion: Borderline ovarian carcinomas are often diagnosed intra- or postoperatively. Preoperative prediction by RMI has poor predictive value. Conservative surgery is to be considered in patients of young age and those who desire fertility preservation.
Poster Session I

LATE RELAPSED OVARIAN CANCER

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Background: The majority of patients with ovarian cancer relapse within 2 years of diagnosis. However, a minority of patients have a long time to relapse of > 5-years after initial diagnosis.

Aims: We identified 13 patients from a computerised-database treated at UCLH, London UK, who had relapsed 5-years or more from their initial diagnosis.

Methods: Case notes of thirteen patients were reviewed and retrospective analysis performed. All cases were discussed at local Multi-disciplinary meetings. All 13 patients were biopsied at relapse to confirm recurrence of ovarian cancer and exclude a second/new primary.

Results: 3 patients had FIGO stage I (Ia n=2, Ic n=1), 9 patients had stage III disease and original stage unknown for 1 patient. Median time to relapse (initial diagnosis-relapse) was 80.79 months (6.73 years) (range = 60-144 months). 2 patients had complete resection of recurrent tumours without any further treatment, 1 patient had resection and then chemotherapy and 1 patient had a failed resection. 11 patients received chemotherapy for recurrent ovarian cancer with mean number of courses received being 2 (range 1-5): 6 patients received carboplatin-paclitaxel, 1 carboplatin-caelyx and 4 had carboplatin monotherapy. There were 4 CR, 1 PR, 2 SD, 3 PD and 1 patients’ response was unknown. 4 patients had third-line chemotherapy and 1 patient had 4 lines of chemotherapy. Median OS time (relapse-death) was 85.06 months (6.67 years) with median follow-up of 28.5 months from relapse.

Conclusions: Ovarian cancer can remain dormant for prolonged time periods with late recurrences even >5-years after initial diagnosis.
Poster Session I

PLATINUM RESISTANCE IN NEOADJUVANT CHEMOTHERAPY COMPARED TO PRIMARY SURGERY IN PATIENTS WITH ADVANCED EPITHELIAL OVARIAN CARCINOMA

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Objective: Compare response to chemotherapy in patients that received neoadjuvant chemotherapy with interval debulking surgery (NACT-IDS) vs. primary debulking surgery (PDS).

Methods: From our Cancer Registry database we identified patients with stage IIIC and IV ovarian cancer who underwent treatment from 2005 to 2010. Standard univariate analyses were performed, as were multivariable analysis with logistic regression. The Kaplan-Meier method was used to generate survival data.

Results: The study population consisted of 425 patients. The median age of the study population was 62 years. 95 (22.3%) women underwent NACT-IDS and 330 (77.6%) PDS. The rate of patients optimally debulked to < 1 cm residual disease was higher in NACT-IDS compared to PDS (91.5 vs. 82.7%; p=0.04). NACT-IDS patients were more likely to be platinum resistant at 6 months (44.2% vs. 31.2%; p=0.01). When multivariate logistic regression was used to control for factors independently associated with platinum resistance (age, residual disease, stage), NACT-IDS was no longer associated with an increased risk of platinum resistance. There was a difference in median overall survival between NACT-IDS and PDS (42 months vs. 60 months; p=0.01). In the Cox regression analysis, optimal cytoreduction (p < 0.001), platinum and taxol based chemotherapy (p = 0.002), and stage (p = 0.01) were independently associated with survival. Age (p = 0.2) and NACT-IDS (p = 0.07) failed to show statistical significance.

Conclusions: After controlling for factors independently associated with platinum resistance, NACT-IDS was not associated with an increased risk of platinum resistance.
**Poster Session I**

**EGF-R INDEPENDENT REGULATION OF E2F3A BASED ON MIR-34A PROMOTER METHYLATION AND 6P22 AMPLIFICATION RELEVANT IN BYPASSING EGF-R-TARGETING IN OVARIAN CANCER**

D. Reimer¹, H. Kiefel², M. Hubalek¹, E. Müller-Holzner¹, M. Erde³, H. Fieg¹, C. Marth¹, P. Altevogt², A.G. Zeimet¹

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**Background:** EGF-R mediated regulation of proliferation promoting transcription factor E2F3a is pivotal in the tumorbiology of ovarian cancer. Herein we give evidence of two distinct mechanisms of EGFR independent regulation of E2F3a bypassing EGF-R signaling.

**Methods:** Status of miR-34a promoter methylation was assessed by means of MethyLight-PCR. MiRIDIAN® based knockdown/induction of miR-34a was performed in cell lines and 6p22 amplification status in cell lines and primary tumor specimens was assessed by FISH analyses. Clinical relevance of E2F3a, miR-34a and 6p22 amplification was evaluated in a large collective of 130 ovarian cancer patients.

**Results:** E2F3a expression, which was shown to correlate with aggressive tumor behaviour, retained independent prognostic significance for disease free and overall survival. E2F3a induction was mediated in a large number of cancer specimens (89%) by EGF-R activation which was evidenced by a highly positive correlation between E2F3a over-expression and phosphorylated EGF-R. However, 11% of tumors indicate E2F3a induction based on miR-34a promoter methylation and/or 6p22 gene locus amplification. Knock-down or induction of miR-34a evidenced a direct regulatory link between miR-34a and E2F3a, and the tumor-suppressive character of miR-34a was documented by its inverse correlation with grading, residual disease and association with improved survival. 6p22 gene amplification was detected in 35% of ovarian cancer specimens and correlated with grading and FIGO stage.

**Conclusion:** These clinical findings highlight the relevance of E2F3a in the biology of ovarian cancer. Moreover, identification of EGFR-independent mechanisms in E2F3a control can be helpful in explaining non-responsiveness of therapeutic EGF-R targeting in ovarian cancer.
SUBOPTIMAL MANAGEMENT OF LAPAROSCOPICALLY OPERATED OVARIAN CANCER PATIENTS-UNDEREPORTED ISSUE


1st Dpt of Ob-Gyn, Gynecologic Oncology Unit, Athens University, Athens, Greece

The aim of this study was to assess the impact of laparoscopy as a surgical approach to ovarian cancer patients.

A retrospective chart review was undertaken of 46 ovarian cancer patients who initially underwent laparoscopic surgery for a presumed benign ovarian tumor between 1999 and 2010.

All patients were referred to our Unit for further surgical management meaning a thorough staging laparotomy. In 9 cases a TAH and BSO due to advanced stage disease and in 4 other a biopsy of the contralateral ovary due to abnormal findings were also performed.

All cases were laparoscopically operated by gynecologists with no oncologic background. The mean age of the patients was 32.6 years (range, 24-43). Time from initial laparoscopy to staging laparotomy was ranged from 19 to 34 days (mean 20.5). An upstaging from apparent stage IA to stages IC to III was found in 31 patients (67.4%). The rest 15 cases with no extraovarian disease were managed as stage IC due to tumor rupture or morcellation during laparoscopy. There were 8 patients (17.3%) with documented disease progression in either port sites or into the peritoneum. All patients received Taxol and Carboplatinum based chemotherapy (4-8 cycles).

In 16 patients (34.7%) adjuvant chemotherapy and in 8 patients (17.3%) disease upstaging could be avoided if laparoscopy wasn’t used as initial approach.

In conclusion we suggest that in cases of ovarian malignancy laparoscopy could have a possible detrimental effect due to delayed staging, tumour spillage and lack of oncologic experience of the physicians involved.
Poster Session I

BUDGET IMPACT ANALYSIS FOR A REGIONAL HEALTH CARE SERVICE PROVIDER AFTER INTRODUCTION OF HE4 TESTING FOR PELVIC MASS DIAGNOSIS

C. Romagnolo¹, T. Maggino², M. Gion³, P. Berto⁴


Background and aims: Ovarian cancer leads to 3000 deaths annually in Veneto Region of Italy (PNLG, 2004[1]). The utility of HE4 (Human epididymis protein 4) in diagnosis of ovarian cancer was studied by several groups as either a single diagnostic marker or in combination algorithm with CA125. In these studies HE4 showed a negative predictive value (NPV) of 99% indicating that almost all patients with negative test results and benign ovarian pathology were correctly diagnosed (2,3). The objective of our study was to perform a budget impact analysis (BIA) and estimate the annual cost for Regional Health Service in Veneto, Italy after the introduction of HE4 testing for differential diagnosis of women with pelvic masses.

Methods: The study compares the cost of surgical intervention versus the preoperative use of HE4 test for pelvic mass diagnosis. The estimates of the incidence of pelvic masses, surgical interventions and costs for both procedures (HE4 and surgery) were based on the available statistical data and reimbursement rates in Veneto Region, Italy.

Results and conclusions: Table 1. shows the annual estimated costs for HE4 testing and pelvic mass surgeries and budget impact after HE4 test introduction. If HE4 testing was performed in all potentially eligible women for preoperative pelvic mass evaluation (1st test) and as an additional follow up test (2nd test) in women who tested negative and avoided surgery, a conservative estimate of 10% reduction of surgical interventions would have a cost-neutral or even slightly positive impact on annual budget in Veneto, Italy.

<table>
<thead>
<tr>
<th>Estimates for Year 2012</th>
<th>HE4 Test</th>
<th>Surgical intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nº patients</td>
<td>32,288</td>
<td>3723</td>
</tr>
<tr>
<td>Cost/patient</td>
<td>€ 35</td>
<td>€ 3132.15</td>
</tr>
<tr>
<td>Cost / all eligible patients</td>
<td>€ 1,130.075</td>
<td>€ 11,660.978</td>
</tr>
<tr>
<td>Nº Avoided Surgery</td>
<td>10%</td>
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</table>

<table>
<thead>
<tr>
<th>Estimates for Year 2012</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic Mass Surgery</td>
<td>€ 11,660.978</td>
<td>€ 10,494.880</td>
</tr>
<tr>
<td>HE4 1st test</td>
<td>-</td>
<td>€ 1,130.075</td>
</tr>
<tr>
<td>HE4 2nd test (follow-up)</td>
<td>-</td>
<td>€ 13,031</td>
</tr>
<tr>
<td>Total Cost</td>
<td>€ 11,660.978</td>
<td>€ 11,637.986</td>
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<tr>
<td>Savings</td>
<td>-€ 22,992</td>
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</tr>
</tbody>
</table>

[Table 1]
Poster Session I

TUBULIN-Β-III OVEREXPRESSION IS A MARKER OF SENSITIVITY TO EPOTHILONES IN OVARIAN CLEAR CELL CARCINOMA

D.M. Roque¹, S. Bellone¹, C. Romani², N. Buza³, E. Cocco¹, S. Gasparini¹, E. Bignotti², A. Ravaggi², T.J. Rutherford¹, P.E. Schwartz¹, S. Pecorelli³, A.D. Santin¹

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Introduction: Compared to ovarian serous papillary carcinomas (OSPC), ovarian clear cell carcinomas (CCC) are associated with an aggressive clinical course and chemoresistance. Tubulin-β-III overexpression prognosticates poor clinical outcome in a variety of cancers but has been incompletely described in CCC. Epothilones are microtubule-stabilizing agents with potential activity in paclitaxel-resistant malignancies.

Objectives: To characterize in vitro chemosensitivity to paclitaxel/patupilone in relationship to tubulin-β-III expression in CCC versus OSPC

Methods: Tubulin-β-III was quantified by RT-PCR in fresh-frozen specimens (26-CCC/35-OSPC) and cell lines (4-CCC/7-OSPC) and correlated with immunohistochemistry (IHC) (4-CCC/9-OSPC). IC₅₀ was determined in 6 cell lines (3-CCC/3-OSPC). Impact of tubulin-β-III knockdown on IC₅₀ was assessed using siRNAs.

Results: Table 1 illustrates source patient characteristics. CCC overexpressed tubulin-β-III relative to OSPC in fresh-frozen tissues and cell lines (Figure 1a/b). IHC reflected RT-PCR copy number (Figure 2; mean 2+ to 3+ versus 0 to 1+, p=0.05). Relative to OSPC, CCC were more sensitive to patupilone (IC₅₀ 0.06±0.01 versus 1.01±0.13 nM, p=0.01) (Figure 3a); this correlated with copy number (Figure 3b). Knockdown of tubulin-β-III enhanced sensitivity to paclitaxel (Figure 3c).

Conclusions: Ovarian CCC overexpress tubulin-β-III relative to OSPC and are exquisitely sensitive to patupilone. Tubulin-β-III functions as a marker for sensitivity of CCC to patupilone and may confer resistance to paclitaxel. Epothilones represent a promising treatment for ovarian CCC.
Table 1: Source patient characteristics for fresh-frozen tissue samples.

<table>
<thead>
<tr>
<th>Stage</th>
<th>CCC (n = 24)</th>
<th>%</th>
<th>OSPC (n = 35)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>13</td>
<td>50.0</td>
<td>3</td>
<td>8.6</td>
</tr>
<tr>
<td>Advanced</td>
<td>12</td>
<td>46.2</td>
<td>31</td>
<td>88.6</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>3.8</td>
<td>1</td>
<td>2.3</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Histology</th>
<th>CCC (n = 24)</th>
<th>%</th>
<th>OSPC (n = 35)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure</td>
<td>19</td>
<td>73.1</td>
<td>35</td>
<td>100.0</td>
</tr>
<tr>
<td>Mixed component</td>
<td>7</td>
<td>28.9</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Race</th>
<th>CCC (n = 24)</th>
<th>%</th>
<th>OSPC (n = 35)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>25</td>
<td>96.2</td>
<td>33</td>
<td>94.3</td>
</tr>
<tr>
<td>Black</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
<td>5.7</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>3.8</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age, mean [range] (y)</th>
<th>CCC (n = 24)</th>
<th>%</th>
<th>OSPC (n = 35)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63</td>
<td>[34-85]</td>
<td>60</td>
<td>[24-90]</td>
</tr>
</tbody>
</table>

Figure 1: Ovarian clear cell carcinomas (CCC) overexpress tubulin β-3 relative to ovarian serous papillary carcinomas (OSPC) in both [a] fresh frozen tissues and [b] cell lines.
Figure 2: IHC staining correlates with tissue expression as determined by RT-PCR. Representative slides are shown in relationship to copy number at high and low magnification.
Figure 3: [a] Ovarian clear cell carcinoma (CCC) is highly sensitive to patupilone. Representative dose-response curves and IC\textsubscript{50} values as determined by flow cytometry after exposure to drug for 72 hours in CCC cell lines are shown. IC\textsubscript{50} values (mean ± SEM) for patupilone among OSPC (not shown) and CCC cell lines are 1.01 +/- 0.13 and 0.06 +/- 0.01 nM, respectively (p = 0.01). [b] Tubulin-β-III copy number correlates with sensitivity to patupilone. [c] Tubulin-β-III knockdown increases sensitivity to paclitaxel. Average values across CCC-1, CCC-2, CCC-3 are shown; error bars represent SEM.
Poster Session I

NACT IN EOC PATIENTS SELECTED FOR HIPEC PROCEDURE

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Background and aims: Neoadjuvant chemotherapy (NACT) in patients with epithelial ovarian cancer (EOC) followed by interval cytoreductive surgery (CRS) is not inferior to primary CRS followed by chemotherapy as a treatment in advanced disease (1). We adopted NACT before CRS in association to hyperthermic intraoperative peritoneal chemotherapy (HIPEC) (2). This clinical approach could have various advantages specially using NACT to select chemosensitive patients and thus offering HIPEC to those highly responders.

Methods: We began a prospective observational pilot study in 8 patients with advanced EOC combining CRS and HIPEC in upfront setting to NACT in chemo-responder patients.

Results: 8 patients with EOC were enrolled in the pilot study. Clinical response to NACT (cisplatin and paclitaxel) was complete in 3 patients and partial in 5 cases. All patients underwent CRS resulting in Complete Cytoreduction (CC0) disease. Supramesocolic peritoneectomy was required in 4 patients and 5 patients underwent colorectal resection. All patients underwent HIPEC with cisplatin 100 mg/m2 and paclitaxel 175 mg/m2 of body surface area at 42 °C. No postoperative mortality was observed. One patient experienced a grade 3 postoperative complication. All patients are alive, with a mean follow up of 9 months. Seven patients are disease-free at follow up. One patient showed a raising Ca 125 after 10 months of follow up.

Conclusions: This encouraging pilot study confirms the existing data in the literature and has led us to start enrollment of patients in a multicenter phase 3 prospective RCT (CHORINE), comparing CRS + HIPEC vs. CRS alone in Stage IIIC unresectable EOC with partial or complete response after 3 systemic cycles of NACT.
Poster Session I

INTERVAL DEBULKING IN ADVANCED OVARIAN CANCER: SANTA CASA SÃO PAULO EXPERIENCE

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Introduction: Ovarian cancer has the highest fatality rate among gynecological tumors; in Brazil about 3500 new cases/year, with 2000 deaths/year, are estimated. Primary debulking surgery has been the standard of care in advanced ovarian cancer. However neoadjuvant chemotherapy followed by interval debulking has been developed showing similar survival but with lower morbidity and mortality.

Objective: Analyze the interval debulking in patients with advanced ovarian cancer in our institution.

Methods: In the period from September 2004 to January 2010, after approval of the Committee of Ethics in Research of Santa Casa de Misericórdia de São Paulo (Protocol number 424/06), we carried out a prospective study of 40 patients with advanced ovarian cancer (IIIC or IV) initially submitted to laparotomy during which non-resectable disease was diagnosed and a biopsy was performed. Irresectability criteria were based on the Institute Gustave-Rousy, which were the presence of at least one of these factors: resection of more than three segments of intestine, plenopancreatectomy, liver resection, presence of lymph nodes larger than 2 cm, "frozen pelvis", diffuse carcinomatosis or invasion of the root of the mesentery. We employed a neoadjuvant chemotherapy protocol with paclitaxel 175 mg/m² and carboplatin AUC 5 every 21 days in three cycles. In the sequence, patients were examined and evaluated by abdomen and pelvis CT and CA 125 dosage. In the absence of disease progression, patients were subjected to interval laparotomy with the goal of optimal cytoreduction.

Results: Optimal cytoreduction was possible in 28 patients (70%) with morbidity and mortality from 5% and 2,5% respectively. The overall survival at five years was 35%.

Conclusion: The interval debulking is an alternative therapy in advanced ovarian cancer, allowing optimal cytoreduction opportunity to patients with unresectable disease, with acceptable morbidity and mortality. Interval debulking produced similar overall survival as primary debulking followed by chemotherapy.
CLINICAL IMPACT OF BRCA1 GENE METHYLATION STATUS IN HIGH-GRADE SEROUS OVARIAN CANCER (HGSOC) PATIENTS


1Department of Gynecology, Obstetrics and Urology, Sapienza University of Rome, Rome, Italy, 2Department of Gynecology, Charité Medical University Berlin, 3Epiontis GmbH, Berlin, Germany

Background: Mutations in BRCA1/2 genes increase risk for breast and ovarian cancer (OC). Hypermethylation of CpG islands in gene promoter regions is associated with inactivation of tumor suppressor genes and cancer onset. Studies identified methylation changes in OC patients but small cohorts and different histological subtypes were analyzed. Aim of this study was to analyze the clinical impact of BRCA1 promoter gene methylation status in HGSOC.

Methods: The cohort comprised 257 HGSOC treated by cytoreduction plus platinum-based chemotherapy at Department of Gynecology, Charité Medical University Berlin, Germany. Fresh frozen OC tissues from TOC presenting over 50% of tumour area were included. DNA extraction and sodium bisulfite conversion were followed by assessment of BRCA1 gene promoter methylation rate determined by PCR. SPSS software was used for statistical analysis.

Results: 14.8% of patients presented hypermethylation of BRCA1 promoter gene. The hypermethylation was significantly more frequently encountered in the younger patients (< 59 yrs: 71% in Hypermethylation Group vs 47% in Hypomethylation Group, p=0.014). No differences in methylation status between primary and metastatic tissue could be observed. Optimal tumor debulking could be reached in most of the patients (63%), without significant differences between both groups. No correlation with FIGO stage and platinum response rates was observed and no difference in PFS and OS was found.

Conclusions: The study shows that HGSOC patients presenting BRCA1 gene promoter in the methylated status developed OC significantly earlier respect to patients with unmethylated BRCA1 gene promoter. The clinical outcome was similar in HGSOC independently from BRCA1 methylation status.
Poster Session I

SURVIVAL AFTER COMPLETE PRIMARY DEBULKING SURGERY SUPERIOR TO COMPLETE INTERVAL DEBULKING SURGERY IN FIGO STAGE IIIC-IV OVARIAN CANCER

M.J. Rutten¹, J. van der Velden¹, G. Fons¹, H. Trum², W. van Driel³, G.G. Kenter¹, M.R. Buist¹

¹Department of Gynaecology, Academic Medical Centre, ²Department of Gynaecology, VU University Amsterdam, ³Department of Gynaecology, Netherlands Cancer Institute, Center Gynaecologic Oncology Amsterdam, Amsterdam, The Netherlands

Objectives: Achievement of no residual tumour at debulking is goal of treatment in epithelial ovarian cancer (EOC) patients. Neoadjuvant chemotherapy and interval debulking surgery (NACT-IDS) is increasingly used in treatment of EOC to achieve higher rates of debulking without macroscopic tumour. We compared survival of EOC patients treated in our institutions with primary debulking surgery and adjuvant chemotherapy (PDS-AC) or NACT-IDS.

Methods: A retrospective study of all primary EOC FIGO stage IIIC/IV patients treated with either PDS-AC or NACT-IDS in our gynaecologic-oncology centres between 1998 and 2010. Impact of surgery on survival was assessed by Kaplan-Meier and logistic/Cox-regression analyses.

Results: In total 301 EOC patients underwent debulking surgery (45% PDS). Median overall survival of patients without residual tumour was 72 and 33 months after PDS and IDS respectively (p< 0.000). There was no difference in survival of patients without residual tumour after IDS and patients with more than 1 cm residual tumour after PDS (p=0.81). No residual tumour was achieved 1.5 times more often in the NACT-IDS-group. Type of surgery did not affect survival in stage IV patients (p=0.62).

Conclusion: PDS without residual tumour has a better prognosis than IDS with the same surgical endpoint. It is hypothesized that at time of IDS more non-recognized disease is left behind. Therefore we suggest that NACT-IDS should be reserved for patients in whom PDS with maximal effort to remove all visible tumour is impossible. Selecting patients for PDS is of upmost importance.
Survival in FIGO III/IV ovarian cancer patients after PDS or IDS

[Survival EOC PDS versus IDS]
Poster Session I

ROLE OF HLA-G EXPRESSION IN OVARIAN CANCER WITH DOWN REGULATION OF CLASSICAL HLA EXPRESSION

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Background: Loss of classical HLA expression is associated with a poor prognostic outcome in ovarian cancer patients. In addition, expression of HLA-G plays an important role in escape of ovarian cancer cells from host immune surveillance. The aim of this pilot study was to evaluate the prognostic impact of expression of classical and non-classical HLA molecules in ovarian cancer.

Methods: Tissue microarrays (TMA) of formalin fixed paraffin embedded tumour tissue of 111 epithelial ovarian cancer patients were constructed. These were immunohistochemically stained for classical and non-classical HLA. Expression of HLA-A, -B/C, -E and -G was compared with survival using the log rank test with additional Kaplan-Meier curves.

Results: HLA-A positivity was associated with good survival (p=0.019). In patients with serous tumours loss of HLA-A expression was strongly associated with poor survival (p=0.009). When stratifying for HLA-G expression, there was a clear trend towards good prognosis for patients with loss of HLA-A and without upregulation of HLA-G (p=0.09). Especially for endometrioid cancer, HLA-G overexpression was associated with poor survival (p=0.025). No associations were found for HLA-B, C and HLA-E expression.

Conclusion: We found that expression of HLA-A and G is associated with survival in ovarian cancer patients. Further analysis of expression of HLA-G in ovarian tumours with HLA-A downregulation is warranted given the prognostic importance of these molecules in ovarian cancer. We will expand our study to validate these results in a larger cohort.
Poster Session I

PROTECTIVE EFFECTS OF PROPOLIS AGAINST SIDE EFFECTS OF CHEMOTHERAPIC DRUGS IN TREATMENT OF OVARIAN CANCER

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Propolis is a natural product created by mixing sap from Manuka Tree and flower buds with natural beeswax and their saliva and other enzymes. Medical studies have shown that Propolis has a lot of benefits; anticancer, antioxidant, antimicrobial, anti-inflammatory and ext... This study was carried out to find the effects of propolis against side effects of chemotherapic drugs in patients with ovarian cancer, 50 patients who candidated for chemotherapy after ovarian cancer surgery divided in two groups; Group 1 treated with chemotherapy drugs and Propolis, group 2 treated by placebo and chemotherapy. The results showed that the side effects in group 1 were significantly less than group 2 (20% vs 80%).
Poster Session I

TRABECTEDIN (ET-743) SINGLE AGENT IN RECURRENT HEAVILY PRETREATED OVARIAN CANCER PATIENTS

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Objective: To evaluate the efficacy and safety of Trabectedin (ET-743) in recurrent, heavily pretreated ovarian cancer patients.

Methods: Patients with measurable recurrent disease, and at least 2 prior treatments for recurrent disease were eligible. Treatment consisted of Trabectedin (1.3 mg/m², 3-hr infusion, q21) until progression or unacceptable toxicity. The primary end point was the rate of overall response (OR).

Results: Between January 2010 and February 2012, 52 patients were enrolled. Median number of previous chemotherapy lines was 4 (range, 2-6). Twenty patients (38.4%) were platinum resistant/refractory, while 16 patients were partially platinum sensitive (30.7%), and 16 (30.7%) were fully platinum sensitive.

According to the RECIST criteria, partial response was documented in 6 patients (11.5%), while stable disease was found in 26 patients (50.0%), for an overall rate of clinical benefit of 61.5%. Median duration of response was 3 months (range, 2-10), while median duration of stable disease was 5 months (range, 3-16). There was no difference in the rates of response to treatments according to original platinum sensitivity. Progression of disease was documented in 20 cases (38.5%). Median time to progression was 5 months (range, 1-16).

G3/4 neutropenia, anemia, and thrombocytopenia were documented in 22.2%, 36.1%, and 8.3%, respectively. G3/4 non-hematological toxicity included 66.6% asthenia, 11.1% cardiac toxicity, and 13.8% hepatic toxicity.

Conclusions: Trabectedin single-agent could be considered a potential option in the treatment of this subset of patients with a quite high rate of clinical benefit to be balanced with the toxicity profile.
Poster Session I

DOES IN-VITRO CHEMOSENSITIVITY SHOW SYNERGY WHEN COMPARING SINGLE AGENTS TO PLATINUM-BASED COMBINATIONS IN OVARIAN CANCER?

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Background: Platinum drugs are often given in combination clinically for the treatment of primary ovarian cancer. This study investigates whether the synergy that occurs in vivo also manifests itself in the in vitro environment.

Methods: 2,750 consecutive primary ovarian cancer specimens tested between 1/1/2008 to 2/26/2010 were analyzed with a chemosensitivity assay for response to platinum and non-platinum based therapies. Specimens were classified as responsive or nonresponsive based on cell kill rates. The response rate of each non-platinum single agent was then compared to response for that agent in combination with carboplatin to observe synergy in drug sensitivity between single agents and combinations in vitro.

Results: Response rates for carboplatin (n=2131), paclitaxel (n=2123), docetaxel (n=2085), and gemcitabine (n=2188) were 50.94%, 47.40%, 33.96% and 29.70%, respectively. The platinum-based combinations carboplatin/paclitaxel (79.4%, n=2348), carboplatin/docetaxel (69.64%, n=1851), and carboplatin/gemcitabine (63.68%, n=2131) achieved notably higher response rates than all single agents tested. It was also observed that increased response for non-platinum single agents aligned with increased response to the platinum-based doublet.

Conclusion: In vitro response rates mirror clinical data showing response to doublet therapy is significantly higher as compared to single agents, and increased chemosensitivity for single agents align with increased chemosensitivity to doublet therapy containing that agent. This information supports the potential utility of in-vitro tumor response testing in personalizing chemotherapy regimens for ovarian cancer patients.
Poster Session I

DOES THE DURATION OF AN ADJUVANT CHEMOTHERAPY AFFECT THE PROGNOSIS IN PATIENTS WITH OVARIAN CANCER?

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Introduction: In patients with ovarian cancer cycles of chemotherapy regularly are postponed mostly due to hematologic side-effects or reduced general condition. Within the present study we evaluate the impact of the resulting prolongation of adjuvant chemotherapy on the prognosis in patients with ovarian cancer.

Methods: Within a retrospective study, the records of 187 patients with epithelial ovarian cancer were reviewed. All patients underwent primary cytoreductive surgery and received six cycles of a combination of a platin and a taxan as adjuvant chemotherapy. A prolongation of the duration of chemotherapy for at least 21 days (i.e. the duration of a complete cycle) was correlated with clinical pathological parameters and patients’ survival.

Results: In 54 patients adjuvant chemotherapy was prolonged for at least 21 days. The duration of chemotherapy did only correlate with the patients’ age ($p=0.04$), not with tumor stage ($p=0.4$) or postoperative tumor rest ($p=0.6$). In multivariate survival analysis the tumor stage ($p=0.008$), the postoperative tumor rest ($p<0.001$), and a prolongation of chemotherapy of at least 21 days ($p=0.03$) were associated with the progression-free survival.

Discussion: A prolongation of the duration of adjuvant chemotherapy for at least 21 days worsens the prognosis of progression-free survival in patients with ovarian cancer, independently of other prognostic parameters.
Poster Session I

CATUMAXOMAB IN PATIENTS WITH MALIGANT ASCITES DUE TO EPITHELIAL CANCER: RESULTS FOR OVARIAN CANCER PATIENTS FROM THE CASIMAS TRIAL


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Introduction: Aim of the study was to investigate if addition of 25mg prednisolone premedication improves the tolerability of 3-hour catumaxomab intraperitoneal infusion by demonstrating superiority for safety and non-inferiority for efficacy.

Methods: Out of 219 patients enrolled, 109 patients with ovarian cancer were randomized to catumaxomab plus prednisolone (CP) or to catumaxomab (C) alone. Primary endpoint was the composite safety score (CSS), summarizing the worst CTCAE grades for the main TEAEs (pyrexia, nausea, vomiting, and abdominal pain). Co-primary endpoint puncture-free survival (PuFS), overall survival (OS) and time to next therapeutic puncture (TTPu) were analysed.

Results: Median CCS was comparable for both treatment groups (CP: 4.3; C: 4.4). Mean difference was 0.0 (p= 0.930); superiority of CP for safety was not proven. Median PuFS was 60 days for CP (95% CI 28; 110) and 72 days for C (95% CI 35; 85)(p= 0.929). Median TTPu was 110 days in CP and 556[s1] days in C (p= 0.133). Median OS was 147 days for CP and 100 days for C (p= 0.186).

Conclusions: Premedication with 25mg prednisolone did not change the safety profile and had no negative impact on efficacy of catumaxomab. The ovarian cancer results are in concordance with data observed in the pivotal study (Heiss, Int. J. Cancer 127; 2209-2221, 2010). The CSS after 3 h infusion was comparable to the pivotal study using 6 hours. Thus, the robustness of the treatment effect of catumaxomab in malignant ascites is confirmed by two phase III studies.
TOLERANCE LEVELS TO POST-OP CHEMO MARTINEZ RADIATION IN STAGE III OVARIAN CANCER: IT'S NECESSITY

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Background and aims: Stage III ovarian cancers pose problems of early recurrence after post-operative chemotherapy. In a poor socio-economic setting where costly molecules cannot be afforded by Indian patients, radiation by Martinez technique appears to be a viable choice for longer survival. Not enough data or even acceptance is available for role of radiotherapy in late stage ovarian tumors. To observe recurrence and morbidity profile in post radiation cases after six courses of chemotherapy.

Method: Stage III ovarian cancer cases who have received post-operative prescribed chemotherapy as per schedule

ARM -1: Post OP/Chemo + Martinez RT,
ARM -2: Follow up only,
ARM -3: Patients, who had not responded to post operative chemotherapy,

Observation/results: Properly backed up (Indoor observation) patients tolerated post chemo radiation well.

ARM1: 10% had sub-acute intestinal Obstruction, 40% had low counts, 30% had GIT toxicity

ARM2: Recurrence at 6months-12months: Ascites 35%, Pelvic Recurrence 40%, peritoneal residue/recurrence 60%.

ARM-3: 60% had control of progressive symptoms, 30% progressed with symptoms and 20% absconded

Survival 3 year: ARM1: 60%, ARM2: 35%, ARM3: 30%.

Survival at 5 years: ARM 1 -30%, ARM 2- 10%, ARM 3-Nil.

Conclusion: Emergence of rationalized and backed up radiation therapy in late stage ovarian tumors results in prolonged survival with no extra cost on targeted therapy.
Poster Session I

RADIOLABELING OF ANTI-CA125 MONOCLONAL ANTIBODY AND SINGLE CHAIN VARIABLE FRAGMENT FOR MOLECULAR IMAGING AND TARGETING OF EPITHELIAL OVARIAN CANCE

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Objective: Ovarian cancer is characterized by over-expression of mucinous glycoprotein CA125 that serves as a tumor marker. The present work utilizes anti-CA125 monoclonal antibody (mAb) and single chain variable fragment (scFv) to develop targeted radionuclide-based molecular imaging tools to evaluate CA125 expression by positron emission tomography (PET).

Methods: Anti-CA125 mAb was purified from B43.13 hybridoma using protein G affinity chromatography. Anti-CA125 scFv was produced by recombinant expression in E.coli. NIH:OVCAR3 cells (CA125+ve) and SKOV3 cells (CA125-ve) were used for immunostaining and cell uptake studies. N-succinimidyl 4-[18F]fluorobenzoate ([18F]SFB) was used to radiolabel anti-CA125 mAb and scFv. 64Cu was obtained from Washington University (St. Louis, MO). pSCN-Bn-NOTA was used as a macrocyclic chelator for 64Cu labeling.

Results: Anti-CA125 mAb and scFv were purified in yields of 7 mg/L and 0.6 mg/L from cell cultures. Immunostaining with FITC-labeled anti-CA125 mAb and scFv showed specific binding to OVCAR3 cells and no binding to SKOV3 cells. Radiolabeling with 18F provided anti-CA125 mAb and scFv in 20% and 35% radiochemical yields respectively. Radiolabeling with 64Cu provided anti-CA125 mAb and scFv in 72% and 42% radiochemical yields respectively. Radiolabeled anti-CA125 mAb and scFv exhibited high (> 60% ID/mg) and selective uptake in OVCAR3 cells and virtually no uptake in SKOV3 cells. Radiopharmacologic evaluation of these targeting vectors in tumor xenograft models is currently underway.

Conclusion: Radiolabeling of anti-CA125 mAb and scFv using [18F]SFB and 64Cu did not alter their immunoreactivity. This renders them as potential PET probes for targeted in vivo molecular imaging of ovarian cancer.
CHARACTERIZATION AND PROTEOMIC ANALYSIS OF OVARIAN CANCER-DERIVED EXOSOMES

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Exosomes are important intercellular communication vehicles, released by various cell types. Although recent studies have indicated that tumor-derived exosomes play important roles in tumor growth and invasion, the mechanisms of secretion, and the biological roles of ovarian cancer-derived exosomes are not well understood. Here we presented firstly the protein profile of highly purified exosomes derived from two ovarian cancer cell lines, OVCAR-3 and IGROV1. Exosomes were prepared by classic method, including several steps of centrifugation and purified by sucrose/D2O cushion ultra-centrifugation. The proteome of the highly purified exosomes were profiled by 1D SDS-PAGE electrophoresis and LC-MS/MS analysis. Some of identified proteins were confirmed by Western blotting. Exosomes derived from ovarian cancer cell lines were found to be round and 30-200nm in diameter under cryo-electron microscopy. Exosomal marker proteins TSG101 and Alix were detected in exosome preparations derived from OVCAR-3 and IGROV1 cell lines. The range of density was between 1.10g/ml and 1.17g/ml. Total 2230 proteins were identified from OVCAR-3 cell-derived and IGROV1 cell-derived exosomes. Among them, 1017 proteins were identified in both two exosomes including all of the major exosomal protein markers. In addition to common proteins to exosomes of all various origins, we also found that some of these proteins are associated with tumorigenesis and metastasis, especially in ovarian carcinoma. Our data indicate that exosomes released by ovarian cancer cells may play important roles in ovarian cancer progression and may provide a potential source of biomarkers in diagnosis and treatment.
Poster Session I

**BMI1 EXPRESSION IS RELATED TO RESISTANCE OF CHEMOTHERAPY AND RECURRENCE IN EPITHELIAL OVARIAN CANCER**

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Although the continuous progress in debulking surgery and the front-line chemotherapy with platinum and paclitaxel in epithelial ovarian cancer, 70% of the patient still died of their diseases eventually because of the relapse and drug resistance. The cause of recurrence and chemotherapy resistance in these intractable cases are perplexing problems for gynecologic oncologists worldwide. The polycomb group protein B lymphoma Mo-MLV insertion region 1 homolog (Bmi1) is a “stemness” gene which is deregulated in various malignancies. It was reported that Bmi1 expression is correlated with proliferation, apoptosis, self-renewal and Epithelial-mesenchymal transition (EMT). However, the relationship between Bmi1 expression and clinical outcome in ovarian cancer remains elusive. In the current study, we found that Bmi1 expression in metastatic tumors influences the response to platinum and paclitaxel containing chemotherapy and correlated with relapse by immunohistochemical staining. The silencing of endogenous Bmi1 expression results in slow proliferation, morphological transformations and increased sensitivity to paclitaxel (a taxane). We also found that Bmi1 inhibition led to downregulation of type III β-tubulin (βIII-tubulin), a newly recognized subtype of β-tubulin involved in taxane resistance, which can explain the morphological transformation and change in paclitaxel sensitivity. This is consistent with the statistically significant positive correlation detected between Bmi1 and βIII-tubulin expression in a cohort of cell lines and multiple surgical ovarian carcinoma specimens. Our results provide mechanistic links between the oncoprotein Bmi1 and the taxane resistance marker. The abrogation of Bmi1 expression might be an effective strategy to enhance the sensitivity of chemotherapy in recurrent ovarian cancer.
Poster Session I

OVARIAN CANCER CELLS WITH THE CD117 PHENOTYPE ARE HIGHLY TUMORIGENIC AND ARE RELATED TO CHEMOTHERAPY OUTCOME

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Cancer stem cells (CSCs) play an important role in the recurrence and drug resistance of cancer. Isolation and characterization of CSCs from ovarian cancer samples may help to provide novel diagnostic and therapeutic targets in the management of recurrent disease and drug resistance in ovarian cancer. Here, we developed axenograft model in which cells from 14 samples of human ovarian serous adenocarcinoma tissue or ascites were implanted in immunodeficient mice to test the tumorigenic potential of different populations of ovarian cancer cells. We identified and isolated the tumorigenic cells as CD117+Lineage− from three different xenografts. As few as 1000 cells with the CD117+Lineage− phenotype, which comprise < 2% of the xenograft tumor cells, were able to regenerate tumors in a mouse model, a 100-fold increase in tumorigenic potential compared to CD117−Lineage− cells. The tumors that arose from purified CD117+Lineage− cells reproduced the original tumor heterogeneity and could be serially generated, demonstrating the ability to self-renew and to differentiate, two defining properties of stem cells. Furthermore, immunohistochemistry analysis of 25 patients with advanced ovarian serous adenocarcinoma revealed positive immunostaining for CD117 in 40% (10 of 25) of patients. CD117 expression was statistically correlated with resistance to conventional chemotherapy (P=0.027). In conclusion, our study demonstrates that human ovarian cancer cells with the CD117+ phenotype possess the unique properties of CSCs, including self-renewal, differentiation, a high tumorigenic potential and chemoresistance. Future studies designed to target CD117+ cancer cells may identify more attractive and effective therapies for treatment of ovarian cancer.
Poster Session I

EFFECT OF ANTISENSE SURVIVIN RNA ON THE GROWTH OF HUMAN OVARIAN CARCINOMA SKOV3 CELLS IN VITRO AND IN VIVO
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Aim: To study the inhibition effect of antisense survivin RNA on the growth of human ovarian carcinoma SKOV3 cells and the tumorigenic ability of the transfected SKOV3 cells transplanted subcutaneously in nude mice.

Methods: The recombinant vector pcDNA3-SVVas was constructed by directed cloning of fragments of survivin cDNA into the vector. The human ovarian carcinoma SKOV3 cells were transfected with pcDNA3-SVVas by Lipofectamine (SKOV3/SVVas cells). The transfected cells were selected in the medium containing G418 and blank vector pcDNA3 as control (SKOV3/neo cells). The stably transfected cells were further studied by detecting the expression of endogenous survivin protein and the change of apoptosis using immunohistochemistry and flow cytometry. Then the transfected SKOV3 cells were transplanted subcutaneously in nude mice.

Results: The growth of SKOV3 cells transfected with pcDNA3-SVVas were significantly slower than the original SKOV3 cells and those cells transfected with blank vector. The expression of survivin protein decreased and the apoptosis of cells increased in SKOV3/SVVas cells in comparison to that in SKOV3 and SKOV3/neo cells. And the tumorigenic ability of SKOV3/SVVas cells was reduced. 5 of 8 (62.5%) nude mice were found tumor. The growth rate of its tumor became very slow, the first time that tumor can be detected was raised up to 14 days (P< 0.05).

Conclusion: Stably expression of antisense survivin RNA can effectively inhibit the growth of SKOV3 cells and reduce the expression of endogenous survivin proteins, induce the apoptosis of cells. pcDNA3-SVVas may be a valuable therapy methods for the ovarian carcinoma.
Posters Session I

CPG ISLAND METHYLATION AND EXPRESSION ANALYSIS OF CASPASE-8 GENE AMONG WOMEN WITH EPITHELIAL OVARIAN CARCINOMA

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Caspase-8 is major components in the extrinsic apoptotic pathway. The alterations of the expression of this gene during the carcinogenesis will contribute to worse tumor prognostic. Despite great research efforts, the biology of epithelial ovarian carcinoma (EOC) remains poorly understood. This study assesses the methylation of CpG island within the Caspase-8 promoter and gene expression both in cystadenoma tumors and primary and metastatic EOC. DNA and RNA was obtained from women with normal ovarian tissues (n=18), ovarian serous cystadenoma tumors (n=11) and EOC (n=16) using Trizol®. The methylation frequency of the CpG island in the Caspase-8 promoter was assessed using the methylation-specific PCR assay after DNA bisulfite conversion. Quantitative PCR was performed to quantify the relative levels of Caspase-8. The differences between the groups were evaluated using the Mann-Whitney U and Kruskal-Wallis tests as indicated. Hemimethylation of the Caspase-8 promoter was found in 11.8% of the normal ovary samples, 20% of the cystadenoma tumors and 20% of the metastatic EOC while methylation of the Caspase 8 promoter was absent in EOC primary tissues (p= 0.047). The lower Caspase-8 expression level was observed in all tumors groups. Significant differences were observed in the caspase-8 expression levels when compared all ovarian tumor groups (p=0.0289) and between the primary and metastatic EOC group (p=0.0076). In conclusion, promoter DNA methylation was not enough to epigenetic silencing of Caspase-8, suggesting the presence of other mechanisms to gene expression control in EOC, which leads to a better understanding of this complex disease.
Poster Session I

EPGENETIC REGULATION AND PROMOTER METHYLATION OF OVARIAN CANCER STEM CELL MARKER CD133

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Objectives: To confirm epigenetic regulation of the expression of CD133 being considered as a candidate marker of cancer stem cell in epithelial ovarian cancer.

Methods: We used the epithelial ovarian cancer cell line (IGROV and OVCAR8) and the endometrial adenocarcinoma cell line (Ishikawa) for control. We analyzed expression of CD133 in 3 gynecologic cancer cell lines by RT-PCR, quantitative real-time PCR, western blots, and FACS analysis. The CD133 expression was examined in each cancer cell line using ovarian cancer cell lines (OVCAR-8 and IGROV-1) and Ishikawa against GAPDH expression.

Results: The CD133 mRNA expression was shown to be different among the cell lines, the weakest expression in the OVCAR8 and the most strongly expression in the Ishikawa. The methylation degree of the CD133 P2 promoter was observed to have been 61% in OVCAR8, 53% in IGROV-1, and 43% in the Ishikawa cell line. The CD133 expression after the DAC treatment increased in both mRNA and protein. On the contrary, the CD133 mRNA expression after the TSA treatment decreased in all cell lines except OVCAR-8. In addition, in the MSP about CD133 P2 promoter, methylation was reduced after the treatment of each drug.

Conclusions: This study means that cancer stem cell of epithelial ovarian cancer can be regulated epigenetically. With further study, epigenetical regulation of cancer stem cell will be applied in the treatment of epithelial ovarian cancer.
ANTI-TUMOR ACTIVITY OF MELITTIN IN OVARIAN CANCER CELLS

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The aim of current study is to investigate whether melittin, a major component of bee venom, inhibit cell growth through enhancement of death receptor expressions in the human ovarian cancer cell lines, PA-1 and SKOV3. Melittin (0.5-2 µg/ml) suppressed the growth of PA-1 and SKOV3 ovarian cancer cell lines by the induction of apoptosis in a dose dependent manner. Consistent with apoptosis, expression of death receptor (DR) 3 and DR6 was increased in both cancer cell lines, but expression of DR4 was increased only in PA-1 cells. Expression of DR downstream pro-apoptotic proteins including caspase-3, 8, and Bax was concomitantly increased, but the phosphorylation of JAK2 and STAT3 and the expression of Bcl-2 were inhibited by treatment with melittin in PA-1 and SKOV3 cells. Expression of cleaved caspase-3 was increased in SKOV3, but cleaved caspase-8 was increased in PA-1 cells. Moreover, deletion of DR3, DR4, and DR6 by small interfering RNA significantly reversed melittin-induced cell growth inhibitory effect as well as down regulation of STAT3 by melittin in PA-1 and SKOV3 ovarian cancer cell. The results of the current study suggest that melittin induce apoptosis in ovarian cancer cells through enhancement of DR3, DR4, and DR6 expression and inhibition of STAT3 pathway.
Poster Session I

DETECTION OF MICRORNA AS NOVEL BIOMARKERS OF EPITHELIAL OVARIAN CANCER FROM THE SERUM OF OVARIAN CANCER PATIENT

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Purpose: miRNA is an abundant class of small non-coding RNA that acts as gene regulator. Recent studies suggested that miRNA deregulation is associated with initiation and progression of human cancer. But, the information about the cancer related miRNA are almost limited to tissue miRNA. And we supposed that if we can find out specific miRNA that is correlate with ovarian cancer in serum, it may be a good candidate for screening tool of ovarian cancer.

Thus, the aim of this study is to find out specific biomarkers of ovarian cancer, using serum miRNA microarray.

Material and method: Two ovarian cancer patients and a healthy control were included in the study. Total RNA was isolated from serum, tissue and ascites respectively, and analyzed by microarray. We select several miRNAs as target biomarkers that showed consistent regulation tendency through all three specimens and showed greatest range of alteration. After then, we performed qRT-PCR for confirming the availability of the biomarkers.

Results: Total 2222 kinds of miRNAs were identified. 95 miRNAs are down-regulated and 88 miRNAs are up-regulated, consistently through serum, tissue, ascites of the cancer patients. Amongst them, 5 miRNAs (hsa-let-7b, hsa-miR-143, hsa-miR-145, hsa-miR-132, hsa-miR-26a) were significantly deregulated in serum of cancer patients and they showed consistent under-expression in cancer tissue and ascites.

Conclusion: From our result, we suggest that hsa-let-7b, hsa-miR-143, hsa-miR-145, hsa-miR-132, hsa-miR-26a may be a candidate for novel biomarkers in epithelial ovarian cancer.
**Poster Session I**

**EXPRESSION OF HLA CLASS I AND HLA-G IN OVARIAN CANCER**


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**Objective:** Among the different mechanisms by which cancer can escape from the immune system, alterations in the expression of human leukocyte antigen (HLA) class I molecules and aberrant expression of the HLA-G on tumor cells may play a crucial role by impairing the interaction of HLA molecules with the specific receptors of T and natural killer (NK) cells. To delineate the potential role of HLA-G and HLA class I in ovarian cancer, we investigated expression patterns of these molecules in human ovarian cancer cell lines and benign and malignant ovarian tumor tissues.

**Material and methods:** In 10 benign and 33 malignant ovarian tumor tissues, and 5 ovarian cancer cell lines (OVCAR-3, ES-2, PA-1, TOV-112D, TOV-21G), HLA-G expression was determined both at mRNA level by reverse transcriptase-polymerase chain reaction (RT-PCR) and at protein level by Western blotting and immunohistochemical staining. Expression of HLA class I antigen was determined immunohistochemically.

**Results:** Expression of HLA-G proteins in all ovarian cancer cell lines was increased. Immunohistochemical analysis of malignant ovarian cancers revealed expression of HLA-G in 27 of 33 tissue samples. However, HLA-G was not expressed in all benign ovarian tumor samples. HLA class I antigen was down-regulated in 25 out of 33 (75.8%) malignant ovarian cancers, and in one of 10 benign ovarian tumor samples. HLA-G expression and down-regulation of HLA class I antigen were associated either with tumor grade (Spearman’s rho = 0.489, \( P = 0.001 \); Spearman’s rho = −0.347, \( P = 0.015 \)) or disease stage (Spearman’s rho = 0.468, \( P = 0.001 \); Spearman’s rho = −0.392, \( P = 0.005 \)).

**Conclusion:** Our results provide that aberrant expression of HLA-G and down-regulation of HLA class I antigen in ovarian cancer may be one of the ways how the tumor down-regulates host immune response.
Poster Session I

UP-REGULATION OF RHOB IS INVOLVING INHIBITORY EFFECT OF GLUCOCORTICOID ON THE CELL MIGRATION IN OVARIAN CANCER CELLS

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We reported in our previous study that Dex induced the expressions of small GTPase RhoB via glucocorticoid receptor (GR) and up-regulation of RhoB was implicated to be a negative regulator of cell proliferation in ovarian cancer HO-8910 cells. In this study, we further found that 100nM Dex significantly inhibited cell migration of HO-8910 and SKOV3 cells by transwell cell migration assay. Inhibiting the expression of RhoB protein by transfecting RhoB-RNAi could significantly reverse the inhibitory effect of Dex on cell migration in HO-8910, indicating that RhoB is involving the inhibitory effect of Dex on cell migration. We also demonstrated that Dex up-regulated ROCK II expression and increased its activity. Treatment HO-8910 cells with Y-27632, a inhibitor of ROCK I II alone resulted in obviously inhibition of cell migration. Moreover, inhibiting ROCK I II activity by Y-27632 did not reverse, but enhance the Dex-induced inhibitory effect on cell migration.

Taken together, our results provided novel evidence that up-regulation of RhoB, but not ROCK II by Dex is involved in inhibitory effect of glucocorticoid on the migration of ovarian cancer cells.
Poster Session I

THE PROGNOSTIC AND PREDICTIVE VALUE OF COMBINED HE4 AND CA125 IN OVARIAN CANCER PATIENTS

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Introduction: A Risk of Ovarian Malignancy Algorithm (ROMA) based on Human Epididymis Protein 4 (HE4) and CA125 has reported to categorize women with a pelvis mass into high or low risk of ovarian malignancy. Originally, the ROMA score was developed for diagnostic purposes but the clinical application for HE4 for other purposes such as a predictor of survival or platinum resistance has not been extensively investigated.

Objectives: To evaluate the prognostic importance of prechemotherapy combined levels of HE4 and CA125 and the utility of predicting platinum resistance. Furthermore, we wanted to investigate the dynamics of the markers during treatment.

Material and methods: Serum from 170 patients with newly diagnosed ovarian cancer was analyzed for CA125 and HE4 using ELISA assays in a training data set. Patients who had high levels (upper third percentiles) of both HE4 and CA125 were classified as high risk patients. The data were sought validated in an independent dataset of an additional 116 patients. HE4 and CA125 were also analyzed at all cycles of subsequent chemotherapy.

Results: The combination of HE4 and CA125 was highly predictive for both progression-free and overall survival in both univariate and multivariate survival analysis where patients in the upper third percentiles was significantly associated with decreased progression-free survival and overall survival in both the training and in the validation set (p< 0.05 in all analysis).

The positive predictive value for platinum resistance in both the training and validation set was higher for the combination of markers than for single markers. The positive predictive values (PPV) were 66.7 % and 57.1% for combined CA125/HE4, respectively.

Conclusions: The combination of HE4 and CA125 levels at baseline just before initiation of chemotherapy were highly significantly associated with decreased progression-free and overall survival and to some extent with platinum resistance.
Poster Session I

LAPAROSCOPIC SPLENECTOMY FOR ISOLATED RECURRENT OVARIAN CANCER

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Objective: To show the feasibility and safety of laparoscopy in the management of recurrent ovarian cancer isolated to the spleen.

Methods and design: An 85yo G3P003 female presented with a history of recurrent papillary serous ovarian carcinoma for which she had undergone 2 prior tumor cytoreductions and chemotherapy. While undergoing routine surveillance with tumor marker and imaging, her CA 125 was found to be elevated at 41 and CT scan of the abdomen and pelvis showed an isolated 4.5 x 4.9 cm splenic mass with no evidence of lymphadenopathy, ascites or carcinomatosis. She was then consented for laparoscopic splenectomy and tumor debulking.

Results: The patient underwent a laparoscopic splenectomy and partial omentectomy. She had no intraoperative complications. The operative time was 2 hours and 25 minutes. Estimated blood loss was 50 mL. On postoperative day 1 she had elevated troponins and was diagnosed with demand ischemia and then had atrial fibrillation on post operative day 2. Her elevated troponins and atrial fibrillation resolved and she was discharged home on postoperative day 6 with no further sequelae. She has completed 4 out of 6 cycles of topotecan with bevacizumab and is alive with no clinical evidence of disease 6 months postoperatively.

Conclusions: Laparoscopy is feasible and safe in the management of recurrent ovarian cancer isolated to the spleen.
Poster Session I

FERTILITY-SPARING VIDEOLAPAROSCOPIC MANAGEMENT OF AN IMMATURE TERATOMA

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Objective: To demonstrate the feasibility and safety of fertility-sparing videolaparoscopic management of an immature teratoma.

Design: A 25 year-old G0P0 Hispanic female presents with a 4 week history of increasing abdominal girth, bloating and pelvic pain. Physical exam revealed a 30 cm gestational age sized mass. Multiple imaging modalities revealed a large suspicious complex right adnexal mass. AFP was mildly elevated. She was consented for laparoscopic resection of pelvic mass and possible surgical staging.

Results: Patient underwent videolaparoscopic resection of the right adnexal mass, right salpingooophorectomy, left paratubal cystectomy, appendectomy, partial omentectomy and chromopertubation. She had no intraoperative complications. Operative time was 2 hours and 59 minutes. Estimated blood loss was 50 mL. There were no postoperative complications. Final pathology revealed a Grade 2 Immature Cystic Teratoma. She is currently undergoing 3 cycles of BEP (Bleomycin, Etoposide, Cisplatin) regimen.

Conclusions: Fertility-sparing videolaparoscopy is both feasible and safe in the management of an immature teratoma.
Poster Session I

DISTRIBUTION OF GYNECOLOGIC ONCOLOGISTS RELATIVE TO OVARIAN CANCER INCIDENCE AND MORTALITY IN THE UNITED STATES

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Background/aims: Guidelines-based treatment for ovarian cancer (OC) includes the recommendation to receive care from gynecologic oncologists (GOs). The aim of this study is to investigate the feasibility of adherence to this recommendation by mapping GO distribution in relation to new OC diagnoses in the United States (US). We also examine GO distribution and OC mortality.

Methods: OC diagnoses and deaths (2002-2006) in the US were obtained from CDC’s NPCR and NCHS, and NCI’s SEER Program. Addresses for GOs were obtained from the Society of Gynecologic Oncologists (SGO); all data were geo-coded and mapped using Geographic Information Systems (GIS) techniques. Multivariate logistic regression was performed to identify significant relationships.

Results: Incidence rates were highest in rural (mean 19.2 per 100,000), followed by suburban (15.3), and urban counties (14.1, p < 0.0001). GO practices were highest in urban (99.3%), followed by suburban (0.7%), and rural counties (0.0%). Almost half of new OC diagnoses (n=51,139) were in counties with no GOs. OC death rates were higher in counties >25 miles from practicing GOs compared to those within 25 miles of a practicing GO (OR=1.40, CI 1.04-1.89 for counties between 25-50 miles; OR 1.59, CI 1.18-2.15 for >50 miles).

Conclusions: Proximity to GOs is associated with lower OC mortality; however, geographic barriers to GO access exist for many US women. It is unlikely that certain populations of women, especially those in rural areas, are benefiting from treatment by a GO as recommended. GO outreach to rural populations may result in decreased OC mortality.
Poster Session I

EVALUATION OF HUMAN EPIDIDYMIS PROTEIN 4 (HE4) AS TUMORMARKER FOR OVARIAN CANCER

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Background: Ovarian cancer is the leading cause of death of gynaecologic cancer among women. The majority of women are diagnosed with advanced stage ovarian carcinoma. CA125 is the most commonly used tumor marker in the diagnosis of ovarian cancer, but is limited in both sensitivity and specificity. Therefore research has been done to evaluate the use of novel biomarkers alone or in combination with CA125.

Aim: The aim of this study was to evaluate human epididymis protein 4 (HE4) as tumor marker, for the diagnosis of ovarian cancer and the discriminative potential between benign and malignant ovarian tumours.

Methods: In 370 patients (34 benign, 156 ovarian cancer, 180 healthy controls) serum values of CA125 and HE4 were measured at time of diagnosis. Median values and ranges of serum tumor markers were analyzed. Sensitivity, specificity and area under the curve (AUC) for CA125, HE4 and the ROMA score for the diagnosis of ovarian cancer were calculated using receiver operating characteristic (ROC) analysis.

Results: The distribution of CA125 and HE4 divided by groups is shown in figure 1-2.

[Boxplot CA 125]
The AUC in the ROC curve in figure 3 shows the discriminative potential between benign and malignant ovarian tumours.
Conclusion: Our results strongly suggest that serum HE4 has a better diagnostic accuracy for the differentiation between benign tumors and ovarian cancer than CA125.
Poster Session I

ROLE OF RADIATION THERAPY IN TREATMENT OF PRIMARY OVARIAN CANCER

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Radiation therapy so as surgery and chemotherapy is one of the steps in treatment of oncological patients. There was revealed, in ovarian cancer patient the main tumor volume during a long period of time is localized in abdominal cavity without distant metastasis. It was a theoretical background for radiation therapy prescription in ovarian cancer patients, though its role in complex treatment of ovarian cancer is still under discussion.

Aim: The aim of this work is to investigate the adequacy of radiation therapy in complex treatment of ovarian cancer patients.

Methods: There was conducted retrospective analyze of treatment results of 367 ovarian cancer patients. There were 112 patients, who have obtained adjuvant radiation therapy.

Results: There were revealed, in ovarian cancer patients stage II and III, who were treated by radical surgery+chemotherapy, at follow-up during 36 months the relapse was detected in 44.7 and 42.9 \%, respectively. In contrast to patients, who additionally obtained adjuvant radiation therapy, the relapse-rate was decreased for 31.5 and 11.1 \%, respectively.

In case of addition the radiation therapy in ovarian cancer patients stage II and III, whom were performed suboptimal cytoreductive surgery+chemotherapy, at follow-up of 6 month the relapse was detected in 20 and 31.4 \%, respectively, in contrast to 46.7 and 69.0 \% in that patients, who have not obtained adjuvant irradiation.

Conclusion: The radiation therapy has good influence on relapse-free survival in ovarian cancer patients, in case of radical surgery. In case of suboptimal cyto-reductive surgery, adjuvant radiation therapy is sensible only in patients with stage II and III.
Poster Session I

FIMBRIAL PRIMARY FALLOPIAN TUBE CANCER: IS IT MORE AGGRESSIVE?

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We report a case of a 70 y.o., G6P6, presenting with increasing abdominal girth. UTZ showed massive ascites. Peritoneal fluid cytology after paracentesis did not show malignant cells. CT scan, however, showed a right adnexal mass. Ca 125 was elevated. Pre-operative diagnosis was Ovarian Carcinoma. Patient underwent THBSO, total omentectomy, PFC, and tumor debulking. Intra-operatively, a necrotic nodular mass was noted at the fimbrial end of the right fallopian tube (RFT). The histopathology report showed Grade II papillary adenocarcinoma of the fimbriated end of the RFT(FPFTC) with extension to the peritoneum and omentum(FIGO Stage IIIC). She received Paclitaxel and Carboplatin(P+C) for 6 cycles. Her CT Scan and Ca 125 levels were normal after 6 cycles of chemotherapy.

Discussion: Primary fallopian tube carcinoma is rare, accounting for approximately 0.14 - 1.8% of gynecologic malignancies. FPFTC is even rarer, with only 20 cases reported in the literature. FPFTC is argued to be more aggressive than those arising from the ampulla (most common site of PFTC) because of the direct exposure of the cancer cells to the peritoneal cavity. Early onset of metastasis to rest of abdominal organs is common. P+C for 6 cycles is the standard chemotherapy regimen. Long term follow-up of cases will provide data on whether recurrence and survival rates are similar to other PFTC.

Conclusion: FPFTC is a rare entity. Reported cases claim early onset of metastasis to abdominal organs. Follow-up of cases will determine if it has poorer prognosis than other types of Fallopian Tube Cancers.
Poster Session I

OUTCOME OF SINGLE AGENT LIPO-DOX IN PLATINUM RESISTANT OVARIAN CANCER, FALLOPIAN TUBE CANCER AND PRIMARY PERITONEAL ADENOCARCINOMA

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Background and aim: Lipo-doxt is one type of pegylated liposomal doxorubicin that commonly use in some Asian country. However, the efficacy of this drug in treated platinum resistant ovarian cancer, fallopian tube cancer and primary peritoneal adenocarcinoma (PPA) is still limited. To evaluate the outcome of Lipo-doxt in this setting, this retrospective study was conducted.

Methods: Between March 2008 and June 2011, the medical record of platinum-resistant ovarian cancer, fallopian tube cancer and PPA patients who received single agent Lipo-doxt were reviewed. Lipo-doxt were administered 40 mg/m2every 21 days until disease progression but no more than six cycles. The response rate and toxicity were evaluated according to WHO criteria.

Results: 24 patients who met the inclusion criteria were reviewed. Most of them were diagnosed as ovarian cancer. Almost patients received Lipo-doxt as the second and third line treatment. The overall response rate was 16.7%. The median time to progression was 11 months and overall survival was 13 months. With the total 74 cycle of Lipo-doxt, grade 3/4 leukopenia and neutropenia were observed in 8.3% and 33.3%, respectively. GCSF was used in 14.9%.

Conclusion: Single agent Lipo-doxt revealed modest efficacy in treated patients with platinum-resistant ovarian cancer, fallopian tube cancer and PPA without serious toxicity.
Poster Session I

RESULTS OF THE TREATMENT OF PATIENTS WITH RECURRENCES OF DISSEMINATED OVARIAN CANCER

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Aim: To improve the results of complex treatment of patients with disseminated ovarian cancer (OC).

Materials: Results of the treatment of 461 patients. Patients were divided into 2 groups according to treatment: Group 1 - 108 (23.4%) patients with recurrences of OC, who undergone combined treatment including a second cytoreduction surgery and chemotherapy (CT) of II line, Group 2 - 353 (76.6%) patients who received only chemotherapy of II line.

Results: In group 1 patients with recurrences of OC the duration of retention of the treatment effect depended on the type of surgery and was 14.3 - 21.6 months after optimal operation; 9.9-12.9 after suboptimal and 7.4-9.3 after non-optimal. In group 2 patients it was depend on tumor stage, the clinical tumor response to CT was significantly lower in patients with stage IV compared to patients with stage III, disease progression during treatment was observed in 54.8% of patients with stage IV patients, in 10.3% - with stage III. In OC patients with stage III complete tumor regression was achieved in 24.2%, partial regression - in 27.6%, the stabilization of process - in 37.9% of patients and in recurrent OC of stage IV - 16.1%, 9.7% and 19.4%, respectively (p < 0.05).

Conclusions: These results indicate that repeated operations can be effective for patients with recurrences of metastatic OC, but it requires careful selection of patients based on a comprehensive examination of the abdominal cavity using endoscopic and radiological methods to determine the criteria for operability.
Poster Session I

OUTCOMES AND PATTERNS OF SECONDARY RELAPSE IN PLATINUM-SENSITIVE OVARIAN CANCER: IMPLICATIONS FOR TERTIARY CYTOREDUCTIVE SURGERY

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Background: Optimal management of platinum-sensitive relapsed ovarian cancer (PSROC) remains unclear. In this case-control retrospective study, outcomes and patterns of secondary relapse in patients with PSROC were evaluated.

Patients and methods: Cases comprised of 83 patients undergoing tertiary cytoreductive surgery (TCS) followed by chemotherapy and controls consisted of 76 patients receiving chemotherapy alone were retrospectively reviewed. Univariate and multivariate analyses were performed to analyze outcomes.

Results: The median survival was 20.3 months in 159 patients. Multivariate analysis identified progression-free interval after secondary cytoreduction (SCR) \((P=0.005)\), mesenteric lymph node metastasis at SCR \((P<0.01)\) and treatment arms at second relapse \((P=0.037)\) as independent predictors of overall survival. Patients with mesenteric lymph node metastasis at SCR had a worse outcome, with a median survival of 11.9 months when compared with 23.3 months in patients without such relapse \((P=0.001)\). TCS improved survival in patients with recurrent disease in the pelvis, when compared with those with recurrent disease in the middle and upper abdomen, with a median survival of 34.9 months, and 14.6 months, respectively \((HR 2.94, P=0.010)\). But it was not a survival determinant found in multivariate analysis. Patients with microscopic residual disease after TCS had a median survival of 32.9 months, compared with 14.6 months in those with macroscopic cytoreduction \((HR 2.82, P=0.001)\), and 15.0 months in patients with chemotherapy alone \((HR 2.23, P=0.001)\).

Conclusion: Limited survival benefit from tertiary cytoreduction was observed in patients with relapsed ovarian cancer. Progression-free interval after secondary cytoreduction was an independent survival determinant.
Poster Session I

A MATCHED CASE-CONTROL STUDY OF DIAPHRAGMATIC PERITONECTOMY IN BULKY STAGES IIIC AND IV OVARIAN CANCER


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Background: Outcomes and complication for patients with bulky stages IIIC and IV undergoing diaphragmatic surgery were evaluated.

Patients and methods: Patients with tumor involving the diaphragm were designed for intention-to-treat from June 2009 to February 2011. Study arm consisted of 32 cases undergoing diaphragmatic surgery, physician-matched controls comprised of 39 cases without diaphragmatic procedure.

Results: Patients undergoing diaphragmatic surgery acquired better optimal cytoreduction (residual disease < 1cm) than those without such surgical procedure (93.7% versus 71.8%, P=0.000). Moreover, 13 (40.6%) patients achieved microscopic residual disease after diaphragmatic surgery. The most frequent post-operative complication was pleural effusion, observed in 6 patients (18.8%), which required chest tube placement or thoracocentesis. The median follow-up was 21.7 mos. (rang, 4.2-36.8 mos.). Nineteen patients (59.4%) recurred in study group, while 26 patients (66.7%) in control group. The median progression-free survival was 19.9 mos. and 15.4 mos. for the study arm and control arm, respectively (HR: 0.609, P=0.092). One year- and 2-year cancer-specific survival were 96.8% and 84.6%; 88.7% and 64.2% for the study group and control group, respectively. Diaphragmatic peritonectomy had a trend to prolong overall survival when compared with control group (mean survival: 33.7mos versus 27.1mons, HR: 0.374, 95% CI 0.118-1.181; P=0.081).

Conclusion: Surgical procedures to clearance diaphragm disease increase the rate of complete and optimal debulking in ovarian cancer. More time needs to follow-up the patients and demonstrate survival benefit from diaphragmatic peritonectomy.
Poster Session I

PLATELET TO LYMPHOCYTE RATIO AS A PROGNOSTIC FACTOR FOR EPITHELIAL OVARIAN CANCER

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Aim: To determine whether preoperative platelets to lymphocyte ratio (PLR) could predict disease stage, result of surgery, and survivals of epithelial ovarian cancer (EOC) patients.

Methods: Medical records of EOC patients who had surgery between January 1, 2004 and December 31, 2010 in our institution were reviewed. Clinicopathological and complete blood count data were recorded. The optimal diagnostic performances of PLR to predict advanced stage, suboptimal surgery, and survival was determined and compared with those of thrombocytosis (≥ 400,000 cells/mm$^3$) and NLR ≥ 2.6.

Results: 166 EOC patients were included in the study. PLR of 200 yielded the best diagnostic performance compared to those of thrombocytosis and NLR ≥ 2.6. The AUC, sensitivity, specificity, positive predictive and negative predictive values, and accuracy (95% confidence intervals [CIs]) of PLR to predict advanced stage were: 0.66 (0.59-0.73), 59% (51-66%), 73% (66-80%), 66% (58-73%), 67% (60-74%), and 66% (59-73%), respectively. The corresponding values to predict suboptimal surgery were: 0.70 (95% CI, 0.62-0.78), 70% (63-77%), 70% (63-77%), 50% (42-58%), 84% (79-90%), and 70% (63-77%). The 5-year PFS and 5-year OS were 53.5% (95% CI, 43.3-63.7 %) and 60.4% (95% CI, 50.4 -70.4%), respectively. Stage of disease, grade of tumor, result of surgery, thrombocytosis and PLR were significant prognostic factors for survivals by univariable analyses while only stage of disease remained significant by multivariable analysis.

Conclusions: PLR was the best prognostic indicator for EOC compared to thrombocytosis or NLR > 2.6. However, its prognostic role could not be confirmed as independent prognostic factor.
Poster Session I

STAGING OF BORDERLINE OVARIAN TUMOR: PERITONEAL DIRECTED AND RANDOM BIOPSIES

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Background: Borderline ovarian tumor is an epithelial tumor with a low rate of growth and a low potential to invade or metastasize. There are conflicting opinion as to which management is appropriate.

Material and methods: We retrospectively reviewed the records of patients with BOT, who were treated at three Institutions between 1980 and 2012. Data collected included medical and surgery details, pathological findings, FIGO stage and follow up data. Patients with micropapillary pattern were excluded for the high correlation with invasive implants.

Results: Of 156 patients investigated, 30 were younger than 40 years. Mean age at diagnosis was 50.48 years. The stage distribution was Ia in 70.32% patients, Ib in 12.90%, Ic in 9.8%, IIa in 0.65%, IIb in 1.31%, IIc in 1.31%, IIIa in 1.31%, IIIb in 0.65%, IIIc in 1.31%. The most common histotypes were the serous (95/176), followed by mucinous (54/176). Peritoneal washing, hysterectomy with bilateral salpingo-oophorectomy, omentectomy and multiple peritoneal biopsies were performed in 76 patients, while conservative surgery was performed in 79 patients. Overall peritoneal biopsies were positive in 9.01% (8/88): 14.29% (4/28) in directed biopsies and 6.67% (4/60) in random biopsies. The mean follow up time was 67 months. We observed 8 primary recurrence and 6 secondary. Recurrence rate in conservative and formal staged patients was respectively 6.25% and 3.95%.

Conclusions: Careful inspection of the peritoneal surface should be undertaken to identify peritoneal invasive implants. Random staging procedure does not seem to have a significant impact on the management of patients with BOT.
ANTI-N-METHYL-D-ASPARTATE RECEPTOR ENCEPHALITIS: A REPORT OF 3 YOUNG WOMEN CAUSED BY THE OVARIAN TERATOMA

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Background: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is rare, but occurs most commonly in young females. It is often associated with an ovarian teratoma and induces various symptoms, including personality changes, memory disturbances, convulsions, and respiratory failure. We describe 3 young women with anti-NMDAR encephalitis caused by the ovarian teratoma.

Cases: The 3 patients were aged 17, 24 and 35 years, and presented with fever, headache, and seizures. They were first diagnosed with meningitis or encephalitis. Two of the three patients advanced to respiratory failure requiring mechanical ventilation. In these 2 cases, CT-scans and pelvic MRIs indicated small calcification and fat tissue in the normal-sized ovaries. Then, the patients underwent unilateral salpingo-oophorectomy. The ovaries were grossly normal in appearance, but cross sections revealed the teratomas, which composed of both solid and liquid portions, containing hair and fat tissue. Histologically, the tumors were diagnosed as mature cystic teratomas. NMDAR antibodies were confirmed in the two patient's cerebral spinal fluid, allowing a diagnosis of anti-NMDAR encephalitis. Another patient showed a mild symptom of anti-NMDAR encephalitis, and was diagnosed as an immature teratoma, 10.0 cm in diameter. Two of the three patients experienced slow reversal of the neurological symptoms. A remaining patient (24 y. o.) is still under treatment.

Conclusion: In young patients, anti-NMDAR encephalitis occasionally results in severe symptoms regardless of the small size of the ovarian teratoma. Hence, an accurate diagnosis of ovarian teratoma followed by surgical resection of the tumor is required for the treatment of anti-NMDAR encephalitis.
Poster Session I

ANALYSIS OF TOLERABILITY AND TOXICITY OF INTRAPERITONEAL CHEMOTHERAPY IN ADVANCED-STAGE OVARIAN, PERITONEAL AND FALLOPIAN TUBE CANCERS

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Introduction: Intraperitoneal (IP) chemotherapy for ovarian cancer has been associated with a high rate of grade 3/4 toxicities preventing patients from completing all 6 IP cycles. Despite a major benefit in overall survival, these toxicities have been implicated as the cause of a lack of acceptance and widespread utilization of the IP regimen.

Objective: Evaluate the tolerability and toxicities of the IP regimen at Moffitt Cancer Center (Tampa, FL) for patients with stage IIC-IV epithelial ovarian, peritoneal and fallopian tube carcinomas.

Methods: Using the Moffitt database, we evaluated the outcomes of all patients who underwent primary optimal cytoreduction for stage IIC-IV ovarian, tubal, and peritoneal carcinoma followed by IP chemotherapy consisting of: Day 1, IV paclitaxel over 24 hours; Day 2, IP cisplatin; and Day 8, IP paclitaxel every 21 days for 6 cycles. NCI CTCAE v 3.0 was used to grade adverse events.

Results: We identified 69 patients meeting our inclusion criteria from 2006 - 2011. The most frequent grade 3/4 toxicities were: neutropenia (48%), gastrointestinal (9%), metabolic (9%) and infection (9%). Remaining toxicities occurred in < 5% of patients. Patients received a greater number of cycles/course compared to GOG protocol 172 (4.28 vs. 3.66) with statistical significance (p = 0.0088). There was no improvement in number of cycles/course received over time (p=0.87).

[IP Regimen Tolerability]
Conclusion: By acquiring familiarity with the IP regimen utilized in the GOG protocol 172; our results reveal that tolerability and toxicities appear improved.
Poster Session I

THE IMPACT OF A FAMILY HISTORY OF CANCER ON THE OVARIAN CANCER RISK IN BRCA1 AND BRCA2 MUTATION CARRIERS

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Purpose: To study the additional value of a family history of breast and ovarian cancer on the risk of ovarian cancer as well as the age of onset in BRCA1 and BRCA2 mutation carriers.

Patients and methods: In a prospective single center cohort study we included a consecutive series of 1846 women from 367 different BRCA1/2 families followed-up at the University Medical Center Groningen between 1996 and 2011. The occurrence and age of onset of breast, contralateral breast and ovarian cancer on available family members was recorded. Cox-regression analysis was applied to assess the correlation between risk of developing ovarian cancer and presence and age of onset of relatives with breast and ovarian cancer within the family.

Results: A total of 263 ovarian cancer cases were diagnosed. Risk of developing ovarian cancer was significantly higher among BRCA2 mutation carriers with relatives with ovarian cancer before the age of 50 (HR=2.34, 95% CI=1.18-4.64, p=0.02 when having first-degree relatives affected and HR=2.11 95% CI=1.12-3.98, p=0.02 when having first- or second-degree relatives affected). Family histories including first- or second-degree relatives with breast cancer showed a trend of protection against ovarian cancer, especially in BRCA2 families (HR=0.47, 95% CI=0.34-0.67 in BRCA1 and HR=0.29, 95% CI=0.17-0.51 in BRCA2, p< 0.01).

Conclusion: Our findings indicate that family histories including ovarian cancer at young age doubles the risk of developing ovarian cancer in BRCA2 mutation carriers, while family histories with breast cancer protect BRCA1/2 carriers against ovarian cancer. These results have applied clinical implications.
Poster Session I

VENOUS THROMBOEMBOLISM IN THAI OVARIAN CANCER PATIENTS AT SIRIRAJ HOSPITAL

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Aims: Last decade venous thromboembolism (VTE) was uncommon in Thailand. Life styles have been changed in many Thai women whereas the number of ovarian cancer increased. Malignancy has been described as a risk factor for VTE which significantly affected mortality and morbidity. We aimed to study the incidence and pattern of VTE in Thai ovarian cancer patients to continue quality improving.

Methods: From January 2005 to December 2009, medical records of 993 Thai ovarian cancer patients were retrospectively reviewed for the first episode of VTE in Siriraj Hospital. Thromboembolic events were confirmed with duplex-doppler sonography or other imaging studies.

Results: Forty six patients were diagnosed of VTE, mean age was 54.5 years. The 5 year-cumulative incidence was 4.63 %. VTE occurred 77 % at lower limb, commonly on the left side, 15% in abdominopelvis and 17% in pulmonary. Time-course (mean ± SD) between diagnosis of ovarian cancer and VTE were 4.2±5.1 ; 4.8±4.2 ; and 48.3±56.6 weeks, before cancer diagnosis; during treatment ; and after treatment , respectively. Two cases of pulmonary embolism were fatal after surgery.

Conclusion: The 5 year-cumulative incidence of VTE was 4.63 %. VTE can occur along the course of ovarian cancer , even asymptaptically. Awareness and proper assessment of VTE should be considered in management of Thai ovarian cancer patients.
Poster Session I

METASTATIC OVARIAN TUMORS FROM NON GYNECOLOGIC MALIGNANCIES. A SINGLE INSTITUTION EXPERIENCE

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Background and aims: The ovaries are frequent targets of metastasis for malignant tumors. Distinction between primary and metastatic ovarian tumors is important because misinterpretation of a metastatic tumor as primary may lead to inappropriate management. Aim of this study was to investigate prognostic factors of patients with metastases to the ovaries from non-genital tract organs.

Methods: Patients with pathologically confirmed metastatic tumors to the ovaries, who were treated from January 1995 to December 2007 were recruited in the study. Age at diagnosis, presenting symptoms, size of ovarian metastasis, laterality of metastasis and primary tumor site were analyzed. The 5-year survival rate was also estimated for all patients included in the study.

Results: A total of 30 cases of metastasis to the ovaries were identified. The median age of the study group was 58 years old (range:20-90). Primary colon cancer was identified in 4 (13.3%) cases; gastric 8 (26.6%); appendix 7(23.3%); non Hodgin lymphoma 3(10%), while breast, kidney and peritoneum each contributed 1 (3.3%) case. Tumors of unknown primary contributed 5 (16.6%) of the cases. Krukenberg tumors pathologically characterized by the presence of typical signet-ring cells were found in 9 (30%) patients. The 5 year survival rate after resection of metastatic ovarian tumors from non gynecologic malignancy was 23%.

Conclusions: Metastatic ovarian tumor should always be included in the differential diagnosis of an adnexal mass. Cytoreductive surgery seems to offer a beneficial effect in survival. Furthermore, improvement in quality of life by alleviating the symptoms must be considered.
Poster Session I

SYNCHRONOUS DETECTED PRIMARY OVARIAN AND ENDOMETRIAL CARCINOMA

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Background and aims: To evaluate the clinicopathologic features in patients with synchronous primary carcinomas of the ovary and endometrium.

Methods: Clinical information and pathologic details were collected and analyzed from 30 women with synchronous endometrial and ovarian cancers.

Results: Median age at diagnosis was 51 years. Abnormal uterine bleeding was the most common presenting symptom (50%). More than half (53%) of the patients were premenopausal and 37% never had a pregnancy. Stage I disease was observed in 90 (27/30) and 73% (22/30) of the patients with endometrial and ovarian cancer, respectively. Endometrioid type was the most frequently observed histology for synchronous endometrial and ovarian cancer (n = 18/30, 60%). All patients were surgically staged and adjuvant treatment was considered when required according to our protocols. The mean follow-up period was 6.6 years (SD = 3.0 years), and the cumulative event-free rate for 5 years was 84.2% (SE 7.3%). No significant differences in the survival rates were found according to the histological subtype (p = 0.513). Women with synchronous primary cancers of the endometrium and ovary were generally younger than those developing either one of the above mentioned adenocarcinomas. They appeared to have a favorable prognosis with an estimated overall survival of 84.2% in 5 years.

Conclusions: A gynecologist should always keep in mind the possibility of double primary carcinomas of the endometrium and ovary in a young, premenopausal, nulliparous woman presenting with abnormal uterine bleeding and prompt the patient for further evaluation.
Poster Session I

EARLY OVARIAN CANCER: A RETROSPECTIVE MULTIVARIATE ANALYSIS

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Background and aims: Early stage epithelial ovarian cancer (FIGO IA-IIA) represent 20% of EOC. The aim of this study is to identify the predictive factors for recurrence and survival in these patients.

Methods: 222 patients treated at the Gynecology & Obstetrics Department of University of Brescia were analyzed. Median follow up was 120 months. Kaplan-Meier survival and Cox proportional hazards were used for analyses.

Results: The 10-years OS and DFS were 83% and 80%. Recurrence occurred in 45 patients (20.3%). On multivariate analysis grading, stage and cytology were significant prognostic factors. Better OS and DFS were described in low risk group stages IA-B G1 (OS 98%, DFS 96%) in comparison to others grouped by stages and grades (intermediate risk IA-B G2-3: OS 80%, DFS 84%; high risk IC-IIA: OS 73%, DFS: 67 %). Worst survival was observed in those with a positive cytology versus negative one (OS 62% vs 82%; DFS 46% vs 83%). Iatrogenic capsule rupture worsened DFS (70% vs 83%), but not OS. We described a negative survival in patients over 54 years. In 32 patients treated with conservative primary surgery followed by adjuvant chemotherapy we observed only 1 recurrence and 1 progression. Adjuvant chemotherapy improved survival of patients with stages not IA G1. We observed a positive prognostic role of taxanes, when used in combination with platino.

Conclusions: Age, stage, grade, and cytology are important prognostic factors in early-stage epithelial ovarian cancer patients. The study underlines the primary role of taxanes and the good prognosis of patients treated with conservative treatment.
Poster Session I

NEOADJUVANT CHEMOTHERAPY FOR PRIMARY ADVANCED OVARIAN CANCER


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Aims: Primary debulking surgery before adjuvant chemotherapy is the standard of care for patients with advanced ovarian cancer, but neoadjuvant CT is considered to be an alternative therapeutic approach in stage IIIC or IV disease. We evaluated patients with NACT and its influence on radicality of surgery and OS.

Materials and methods: We evaluated 138 women treated for advanced ovarian cancer of stage FIGO IIIC-IV unsuitable for primary debulking surgery (PDS) because of unresectable tumor or poor performance status. All women underwent a laparoscopic evaluation verifying inoperable ovarian cancer of stage IIIC-IV. After NACT of 3-4 series was given, laparoscopic reevaluation followed. Some of the women not even after 3-4 series could not undergo PDS due to inadequate response. Therefore further 3 series of NACT were administered and laparoscopic reevaluation followed.

Results: Optimal debulking surgery was achieved in 77 patients (55.8%), suboptimal debulking in 16 (11.6%), 22 (15.9%) stayed inoperable. 42% of the patients underwent surgery after 3 series of NACT, 32% after 4 series, 26% after more. The influence of DFI on OS was established. The longer DFI means the better OS. OS was significantly longer in group of patients with optimal debulking surgery. OS was slightly better in group of patients with 3-4 series of NACT in comparison with more series before surgery. The first optimal debulking played an important role in OS (75% vs 19%). The longest OS was founded in group of patients with histological grade 1.

Conclusion: 55.8% of the women underwent radical debulking surgery after NACT despite the extremely severe findings in time of diagnosis. 26% of patients underwent optimal surgery after more than 4 cycles of NACT. The influence of histological grading and DFS on OS was confirmed. OS was statistically different in patients with optimal and suboptimal surgery. The strongest predictor of OS was the complete resection.
Focus on Elderly Patients with Advanced Ovarian Cancer - A Prospective Analysis of the OVCAD Consortium

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Background: Approximately one third of ovarian cancer patients are 70 years or older. Standard therapy including radical surgery and combination chemotherapy has considerable morbidity and specific information regarding treatment reality in elderly patients is limited.

Methods: Patients with primary epithelial ovarian cancer FIGO-stages IIB-IV were prospectively included in this European multicenter study. All patients underwent surgery with the intent of complete cytoreduction and received a platinum-based chemotherapy. Analyses were performed separately for patients < 70 and ≥70 years and then compared regarding clinicopathological variables and prognosis.

Results: A total of 275 patients were included with a median follow up of 36 months. Median age of the total cohort was 58(18-85) years with 47 patients(17.1%) ≥70 years. Age itself was not a prognostic factor for progression free survival(PFS). 30-days mortality-rate after surgery was 3.6% in elderly patients compared to 0.6% in patients < 70. Surgical management was less radical in patients ≥70(e.g. fewer lymphadenectomies p< 0.001) and the percentage of patients with residual disease after surgery was higher(44.7%) compared to younger patients(28.5%, p=0.029) despite similar FIGO-stage distribution. Furthermore, elderly patients were more likely to receive mono-chemotherapy(p< 0.001). Consecutively, outcome was less favorable in patients ≥70 (median PFS 12 vs. 20 months in younger patients;p=0.022 and overall survival 30 vs. 64 months;p< 0.001).

Conclusions: In this prospective multicenter-study, ovarian cancer patients age 70 and older were treated significantly less radical and had an unfavorable outcome compared to younger patients. In context of our aging society, specific trials focusing on elderly patients are therefore highly desirable.
Poster Session I

LONG TERM FOLLOW-UP OF PATIENTS WITH CLEAR CELL CARCINOMA OF OVARY

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Objective: The study aims to evaluate the long-term outcomes of the patients with clear cell carcinoma of the ovary.

Method: 144 patients with clear cell carcinoma of the ovary were treated in a tertiary hospital between 1987 and 2006. All specimens were reviewed by the gynaecological pathologists. The details of the patients were extracted from their clinical notes and the survival data were analysed.

Results: The mean age of the cohort was 48.1 ± 9.8 (range 26 - 81). 10 patients (6.9%) had surgery alone and 132 patients (91.7%) had surgery with adjuvant chemotherapy. The median duration of follow-up was 78.7 months (range 1.0 - 297 months). 28.4% of the patients relapsed and 17.7% had progressive disease. Among those who were properly staged by either laparotomy for operable diseases or by pre-treatment imaging for inoperable diseases treated by neoadjuvant chemotherapy, the 5-year progression-free survival rate of patients in stage I, II, III and IV was 77.8%, 36.4%, 30.8% and 0% respectively (p < 0.001). The 5-year overall survival rate in each stage was 84.2%, 45.5%, 31.3% and 0% respectively (p < 0.001). After adjusting co-factors like age, use of oral contraceptive pills and endometriosis, history of thromboembolism, hypercalcaemia and early stage were independent factor for progression-free survival (p = 0.008, 0.011 and 0.009 respectively) and thrombo-embolism and early stage remained significant for overall survival (p = 0.032 and 0.05 respectively).

Conclusion: Although clear cell carcinoma is an aggressive cancer, patients with early-staged disease had a favorable prognosis.
Poster Session I

EVALUATION OF LOCAL RADIOTHERAPY FOR ISOLATED LYMPH NODE RECURRENCE OF EPITHELIAL OVARIAN CANCER: THERAPEUTIC EFFECT AND SAFETY

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Objective: Isolated lymph node recurrence (ILNR) of epithelial ovarian cancer (EOC) has been reported to have less aggressive progression and favorable outcome, especially when treated with surgery. However, the role of radiotherapy in ILNR is seldom discussed. We sought to determine the therapeutic effects and safety of local radiotherapy for ILNR of EOC, and compare them with those of surgery.

Methods: We reviewed the medical records of EOC patients undergoing surgery or local radiation for ILNR between January 1995 and December 2008. Patient characteristics, feature of recurrence, survival, and treatment-associated morbidity were evaluated and compared according to treatment modality.

Results: Of a total of 33 identified patients, 14 and 19 underwent local radiotherapy and secondary cytoreductive surgery for ILNR, respectively. Optimal cytoreductive surgery was achieved in all patients undergoing surgery, while complete response was achieved in 12 of 14 patients undergoing local radiotherapy. Follow-up time after ILNR ranged from 16 to 124 months (median 59 months). Six patients in the surgery group and 5 in the radiotherapy group died from the disease. The 5-year post-recurrence survival rate was 71.8% and 68.8% in surgery and radiotherapy group, respectively. There was no significant difference in overall survival or progress-free survival between the two groups (P>0.05). The treatment-associated morbidity and toxicity in radiotherapy group was acceptable and comparable to those of surgery group.

Conclusion: Local radiotherapy is a safe and effective procedure in treating ILNR of EOC.
Poster Session I

OVARIAN CANCER ASSOCIATED WITH ENDOMETRIOSIS

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Background and aims: Previous studies have suggested an association between endometriosis and development of ovarian cancer. A study is performed to evaluate the cases of ovarian carcinoma associated with endometriosis.

Methods: The study included patients with ovarian carcinoma associated with endometriosis diagnosed between 2000 and 2011 at Hacettepe University Hospital. A total of 1086 patients who underwent surgical staging for ovarian carcinoma were analyzed retrospectively for the presence of histologically documented endometriosis. The clinical and pathological characteristics of 45 patients associated with endometriosis including histologic subtype and stage were determined.

Results: Ovarian carcinoma was found to be associated with endometriosis in 4.1% (45/1086) of the cases. Of them, 17 (37.8%) had clear cell, 15 (33.3%) had endometrioid, 6 (13.3%) had serous papillary, 4 (8.9%) had mucinous and 3 had mixed type of ovarian carcinoma. Twenty three (51.1%) patients had stage I, 4 (8.9%) patients had stage II and 18 (40.0%) patients had stage III disease. The frequency of coexistence of endometriosis was 25.7% (17/66) for clear cell carcinoma and 9.3% (15/161) for endometrioid cell carcinoma.

Conclusions: Only a small proportion of ovarian cancer cases were found to be associated with endometriosis. Endometriosis was most frequently associated with clear cell and endometrioid types of ovarian carcinoma. Ovarian carcinoma associated with endometriosis tended to present at earlier stages. Ovarian cancer associated with endometriosis seems to represent a distinct disease entity.
Poster Session I

A CASE OF PORT-SITE METASTASIS OF BRENNER TUMOR AFTER A ROBOTIC-ASSISTED BILATERAL SALPINGO-OOPHERECTOMY

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\textbf{Introduction:} A Brenner tumor is commonly regarded as a benign lesion consisting of cells that resemble the transitional epithelium of the bladder and Walthard nests of the ovary. 1-2\% of tumors will undergo malignant change.

\textbf{Case:} 72 y/o G5P5005 post-menopausal female who presented with complaints of abdominal bloating and abdominal discomfort. CT scan revealed a large left ovarian mass and an abdominal ultrasound confirmed a complex cystic mass in the left ovary. CA-125 was WNL. Patient underwent a robotic-assisted bilateral salpingo-oophorectomy with abdominal peritoneal washings. Pathology of the left ovarian mass revealed a histological grade III poorly differentiated malignant Brenner Tumor (stage IC). Post-operative CT scan a month later revealed a suprafascial anterior wall mass at Palmer's Point. Abdominal mass resection was performed concurrent with formal laparoscopic staging of her disease. Pathology returned invasive keratinizing squamous cell carcinoma. Within 5 months from the salpingo-oophorectomy, a second mass was resected from the initial infra-umbilical trocar site with pathological evidence of invasive keratinizing squamous cell carcinoma. An associated enlarging right lung mass was also identified later on follow-up and was biopsy proven squamous cell carcinoma.

\textbf{Conclusion:} The incidence of Brenner tumor is as low as 2-5\% of all ovarian neoplasms. The incidence of port-site metastasis is approximately 1.1\% in malignant gynecological cases. As the trend in minimally invasive technique continues to advance and gain popularity, the minimal risk associated with these techniques when used by an experienced operator outweighs the potential complications that may occur with port-site metastasis in early stage or borderline disease.
HIGHLY SULFATED CHONDROITIN SULFATES, A NOVEL CLASS OF PROGNOSTIC BIOMARKERS IN OVARIAN CANCER TISSUE

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Objective: Clinical decision making in ovarian cancer needs new (prognostic) biomarkers. Although the search for biomarkers has traditionally focused on tumor cells, their surrounding contains important information as well. Glycosaminoglycans, heterogeneous polysaccharides which are abundantly present in the stromal compartment, are indicated in pathological processes including cancer. In this study we investigated a specific glycosaminoglycan motif (4,6-disulfated chondroitin sulfate) for its potential as a prognostic biomarker in ovarian cancer.

Methods: 4,6-disulfated chondroitin sulfate presence was studied immunohistochemically using the single chain antibody GD3G7 on 148 ovarian tumors including benign and malignant tumors, and tumors with low malignant potential. For comparative purposes p53 and Ki-67 were evaluated. X² tests, univariate and multivariate Cox proportional hazards analysis were applied for statistical analysis.

Results: The stroma of malignant tumors showed significantly increased expression of 4,6-disulfated chondroitin sulfate (GD3G7 epitope) compared with benign tumors and tumors with LMP (p-values < 0.000 and 0.002, respectively). Expression of GD3G7 in malignant tumors was significantly correlated with serous subtype, high tumor grade, advanced FIGO-stage and high CA-125 levels. In patients with advanced FIGO stage GD3G7 expression was significantly correlated with incomplete debulking and good response to chemotherapy. GD3G7 surpassed both p53 and Ki-67 in statistical analysis. Multivariate survival analysis revealed GD3G7 expression as an independent predictor for progression free survival.

Conclusion: Glycosaminoglycan motifs may form a new class of biomarkers for (ovarian) cancer, as indicated here for the GD3G7 epitope. Expression of GD3G7 may contribute in therapeutic decision making and constitutes a potential biomarker for poor prognosis.
HIGH CHONDROITIN SULFATE LEVELS IN CYST FLUID OF MALIGNANT OVARIAN TUMORS

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Objective: Improved insight into the molecular characteristics of ovarian carcinomas is urgently needed. A major factor in tumor progression is the tumor cell’s interaction with the micro-environment of which glycosaminoglycans (GAGs) such as chondroitin sulfate (CS) and heparan sulfate (HS) are major components. The composition of ovarian cyst fluid (oCF) represents the tumor tissue, making it an important source to study. Here, we explored oCF of benign and malignant ovarian tumors of different subtypes, grade and FIGO stage for their GAG content focusing on CS.

Methods: GAGs were isolated from 40 benign and 33 malignant oCFs. CS/HS ratios were determined biochemically and CS fine structure was studied on a disaccharide level.

Results: OCF derived from malignant tumors contained significantly higher GAG levels than oCF from benign tumors (p=0.004). Moreover, GAGs from malignant oCF were mainly of CS subtype. OCF from benign tumors contained primarily HS in case of serous and CS in case of mucinous tumors. High grade and advanced FIGO stages showed high GAG levels with a predominance of CS. Different CS-disaccharide profiles were found for benign and malignant tumors. OCF from non-mucinous, high grade and advanced FIGO stage tumors contained low levels of non- and 2-O-sulfated disaccharides and high levels of the UA-GalNAc6S disaccharide.

Conclusion: Malignant oCF contains high levels of GAGs predominantly CS. Corroborating with today’s knowledge of type I and type II tumors, we hypothesize that high levels of CS with altered sulfation patterns may be a key-factor in the tumoral micro-environment during ovarian cancer progression.
Poster Session I

OCCURRENCE OF ENDOMETRIAL ABNORMALITIES IN WOMEN WITH A GRANULOSA CELL TUMOUR - A POPULATION BASED STUDY

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Background and aims: The occurrence of endometrial abnormalities concurrent with granulosa cell tumours (GCT) varies widely (25-65%) and no data exist on this occurrence during long-term follow-up of GCT. The aim of this study was to evaluate the occurrence of endometrial abnormalities in women with GCT, especially in the follow-up.

Methods: All cases of GCT (approximately 1000 women) in the Netherlands between 1991 and 2012 were evaluated for endometrial abnormalities using the Dutch nationwide network and registry of histopathology and cytopathology (PALGA).

Results: Preliminary results (n=720) showed a mean age of 55 years (SD ± 17) at time of diagnosis of GCT. Endometrial cancer was found in 45 (6%), complex/atypical hyperplasia in 68 (9%) and simple/non-atypical hyperplasia in 127 (18%). Long-term follow-up in 337 women without hysterectomy showed that endometrial cancer was found in 1 (0.3%), complex/atypical hyperplasia in 2 (0.6%) and simple/non-atypical hyperplasia in 5 (1.5%). Interestingly, of these 8 women 5 (63%) had recurrent GCT at the time of endometrial abnormality.

Conclusions: The occurrence of endometrial abnormalities during long-term follow-up in women with GCT is extremely low. Therefore, when endometrial pathology is normal at the time of initial diagnosis of GCT, hysterectomy is not recommended.
**Poster Session I**

**WHOLE ABDOMINOPELVIC RADIOTHERAPY (WAPRT) USING INTENSITY MODULATED ARC THERAPY (IMAT) AS PALLIATION FOR CHEMOTHERAPY-RESISTANT OVARIAN CANCER**


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**Aims:** To assess the palliative effect of WAPRT using IMAT in chemotherapy-resistant ovarian cancer patients.

**Methods:** Forty-two patients were treated (33Gy; 22 fractions). At referral, median age and Karnofsky performance score (KPS) was 59y [31 - 76] and 80 [40 - 90]. Disease-related symptoms were: intestinal (sub)obstruction (n=22), pain (n=20), ascites (n=11), and vaginal bleeding (n=2). Median CA125-level was 421U/ml [6-13796]. All patients were heavily pre-treated and platinum resistant. The OS and abdominal progression free survival (aPFS) were calculated from the start, response duration from the end of treatment.

**Results:** Response rates (completed treatments; n=30): table. Median response duration (all symptoms) was 16 weeks [0-139]. Median OS and aPFS for the whole population were 4 months [0-32] and 11 weeks [0-142]. For those who completed treatment median OS and aPFS were 8 months [2-32] and 17 weeks [4-142]. Patients with a KPS≥70 ended the treatment significantly more (p<0.001), had a better OS (8 vs. 1 month; P< 0.05), aPFS (18 vs 3 weeks; p< 0.001) and response duration (22 vs 5 weeks p<0.001).

**Conclusion:** WAPRT offers palliation for peritoneal metastasized ovarian cancer patients and can resolve GI-obstruction for a substantial period. Careful patient selection is mandatory (KPS≥70).

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[Response rates (%).]
POSTER SESSION I

NEOADJUVANT CHEMOTHERAPY IN ADVANCED OVARIAN CANCER: RESULTS FROM A SINGLE INSTITUTION EXPERIENCE

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Objective: Neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) was not inferior to primary debulking surgery (PDS) followed by chemotherapy as a treatment option for patients affected by advanced ovarian cancer (AOC) (Vergote, 2010).

Additional research is needed to set up common selection criteria for neoadjuvant chemotherapy and portray the proportion of patients in which an attempt at primary surgery should be abandoned in favour of NACT.

Methods: Ninety patients with stage IIIC or IV AOC who underwent IDS (because of an unresectable tumor or strong suspicion of suboptimal resectability at staging exams or exploratory laparoscopy or poor performance status) were prospectively collected and compared with a group of 100 patients treated with PDS (for resectable disease) followed by chemotherapy. All patients were treated between 2000 and 2011 by the same team and received platinum based plus paclitaxel chemotherapy adjuvant regimen.

Results: Acceptable cytoreductive surgery (residual disease ≤ 1 cm) was accomplished in IDS and PDS groups in 77.8% (70 of 90) and 47% of patients (47 of 100), respectively.

The rates of bowel resection, blood loss and postoperative morbidity were not significantly different in the two treatment groups. After adjusting for residual disease overall and event-free survival were not different in the two groups.

Conclusions: Survival rates were similar in patients with advanced stage ovarian cancer who underwent IDS or PDS although the patients in the IDS group were negatively selected particularly in terms of lower performance status. IDS can be safely used in unresectable-advanced stage ovarian cancer.
Poster Session I

ENHANCEMENT OF OVARIAN CANCER CHEMOTHERAPY BY DELIVERY OF A TUMOR-TARGETING SALMONELLA-BASED MDR1 SIRNA

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Objectives: To observe the effect of attenuated Salmonella typhi as a tumor-targeting delivery vector for multidrug-resistance gene (MDR1) small interference RNA (siRNA).

Methods: The cisplatin (DDP)-resistant ovarian cancer cell line SKOV-3/DDP was established by treatment with gradually increasing concentrations of cisplatin. MDR1 siRNA expression plasmids that containing short hairpin RNA (shRNA) of MDR1 gene were constructed and transformed into attenuated Salmonella typhi strain SL7207. SKOV-3/DDP cells were incubated with recombinant salmonella and then subjected to analysis of MDR1 expression by Real-time PCR and western blot. SKOV-3/DDP tumor-bearing nude mice were established by injecting BALB/c nude mice subcutaneously with SKOV-3/DDP cells, and were orally inoculated with salmonella carrying MDR1 shRNA and simultaneously injected intraperitoneally with cisplatin. Tumor growth and mouse survival were observed.

Results: Compared with parental cell line, the DDP-resistant SKOV-3/DDP cells expressed much higher level of MDR1. The salmonella strain bearing MDR1 shRNA was able to infect SKOV-3/DDP cells in vitro and suppress MDR1 expression and reverse DDP tolerance of SKOV-3/DDP cells. Oral administration of recombinant salmonella in tumor-bearing nude mice could suppress tumor proliferation and markedly enhance the therapeutic effect of DDP.

Conclusion: Attenuated Salmonella typhi may represent an effective route for in vivo administration of RNA interference therapy against malignant tumors' drug resistance.
Poster Session I

IMMUNE MECHANISM OF THE ANTITUMOR EFFECTS GENERATED BY BORTEZOMIB

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Bortezomib, a proteasome inhibitor, is a chemotherapeutic drug that is commonly used to treat a variety of human cancers. However, the antitumor effects contributed by bortezomib-induced tumor cell immunogenicity have not been fully investigated. In the current study, we investigated the immune-mediated antitumor effects generated by treatment with bortezomib using murine ovarian tumor model. We found tumor-bearing mice treated with bortezomib had CD8⁺ T cell-mediated inhibition of tumor growth. Tumor cell-based vaccines treated with bortezomib generated potent tumor-specific CD8⁺ T cell immune responses with improved therapeutic antitumor effect in tumor-bearing mice while the tumor cell-based vaccines not treated with bortezomib did not. Treatment of tumor cells with bortezomib led to the upregulation of Hsp60 and Hsp90 on the cell surface. However, cell surface expression of Hsp60 is more important than Hsp90 in determining whether or not bortezomib-treated tumor cells can generate tumor-specific CD8⁺ T cells. CD11c⁺ dendritic cells (DCs) that were treated with bortezomib in vitro had enhanced phagocytic activities. In addition, CD11c⁺ DCs from bortezomib-treated tumor-bearing mice had increased maturation. Taken together, our data indicate that bortezomib can render tumor cells immunogenic by upregulating the cell surface expression of HSP60 and HSP90 as well as improve DC function, resulting in potent immune-mediated antitumor effects.
Poster Session I

A NOVEL STRATEGY FOR ADVANCED EPITHELIAL OVARIAN CANCER USING MONOCLONAL ANTIBODY (C595) COMBINED WITH DOCETAXEL IN VITRO AND IN VIVO

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Aim: To investigate the effectiveness of combination treatment with anti-MUC1 monoclonal antibody C595 (MAb C595) plus docetaxel (DTX) in epithelial ovarian cancer (EOC) cell lines in vitro and in an intraperitoneal (i.p) EOC mouse model in vivo.

Methods: The effect of MAb C595 alone or in combination with DTX on EOC cell lines was studied by proliferation, colony, TUNEL and ELISA assays. OVCAR-3 cells were implanted intraperitoneally in female athymic nude mice and allowed to grow tumor and ascites. Mice were then treated with single or combination therapies. Ascites volume, tumor weight, CA125 levels from ascites and survival of animals were assessed. The expression of MUC1, CD31, Ki-67, TUNEL and apoptotic proteins in tumor xenografts was evaluated by immunohistochemistry.

Results: Low-dose MAb C595 (1/2 of IC₅₀) combined with DTX greatly improved efficiency of cell killing in EOC cells and induced apoptosis; the additive effect of MAb C595 was further confirmed in colony forming assays; and cell death following single or combined treatments was associated with the release of cytochrome c and increased caspase-3 activity. MAb C595 alone inhibited i.p tumor growth and ascites production in a dose-dependent manner but did not obviously prevent tumor development. However, combination test significantly reduced ascites volume, tumor growth and metastases.

Conclusions: This combination approach can effectively kill EOC cells in vitro, reduce tumor burden and ascites, prolong survival of animals through induction of tumor apoptosis and necrosis, and may provide a potential therapy for advanced metastatic EOC.
Poster Session I

RECURRENT GRANULOSA CELL TUMORS: TAIWANESE GYNECOLOGIC ONCOLOGY GROUP STUDY

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Objectives: To evaluate the characteristics and outcome of patients with recurrent ovarian granulosa cell tumors (GCTs).

Methods: The clinical and pathologic characteristics, treatment and outcome of patients with recurrent ovarian GCTs were analyzed from eight medical centers in Taiwan under the TGOG (Taiwanese Gynecologic Oncology Group).

Results: A total of 37 patients were recruited in this study, with the recurrent rate of 21% in 176 pathologically confirmed ovarian GCTs. The recurrent sites included the abdominal cavity (83.8%, n=31), with (13.5%, n=5, 2 in liver and 3 in lymph nodes) and without (70%, n=26) other metastases, lymph node with (n=1) and without (n=3) liver, liver (n=1), and bone (n=1). Twenty-seven patients underwent surgery again, followed with (n=18) and without (n=9) adjuvant therapy. Four patients did not undergo the treatment, contributing to one death (25%), compared with other 33 patients did, with four deaths (12.2%).

Conclusions: The most common site of recurrent ovarian GCTs was abdominal cavity. Surgical approach with and without adjuvant was still the most common method for these patients with acceptable outcomes.
Poster Session I

KINASE INHIBITOR SCREENING TO IDENTIFY NOVEL TREATMENTS FOR OVARIAN CLEAR CELL CARCINOMA

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Background: There is much need for alternative treatments of ovarian clear cell carcinoma (CCC), a subtype of ovarian cancer that responds poorly to standard treatment. To identify pathways and novel therapeutic targets for clinical use in CCC, we performed a kinase inhibitor screen with a panel of drugs that included many that were successfully used in Phase 1 clinical trials.

Methods: The kinase inhibitor screen including over 300 compounds was performed on seven CCC cell lines and an isogenic cell line with knockdown of ARID1A, a gene that has been identified to be lost in approximately half of CCC cases. Following a 48hr treatment with the compounds, cells were stained with crystal violet to assess cell viability. Hits were defined as compounds that caused a signal decrease of at least 50% as compared with controls, and compounds were chosen that were specific to killing CCCs and not normal Mouse Embryonic Fibroblasts (MEFs). Confirmatory tests were performed in triplicate with candidate compounds.

Results: After secondary validation, thirteen potential therapeutic kinase targets were identified, including PLK1, GSK-3, and EGFR. Work is currently underway to further assess the compounds with regards to potency and selectivity in culture with the most promising of these compounds being carried forward to assessment in xenograft models.

Conclusions: Preliminary results from this kinase screen indicate that several novel kinase inhibitors may merit consideration as novel agents for the treatment of CCC.
Poster Session I

FAILURE TO RESCUE AS A SOURCE OF VARIATION IN HOSPITAL MORTALITY FOR OVARIAN CANCER


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Background: While the association between high surgical volume and improved outcomes from procedures is well described, the mechanisms that underlie this are uncertain. There is growing recognition that high volume centers may not necessarily have lower complication rates, but rather may be better at rescuing patients with complications. We examined the role of complications, failure to rescue from complications, and mortality based on hospital volume for ovarian cancer.

Methods: The Nationwide Inpatient Sample was used to identify women who underwent surgery for ovarian cancer from 1988-2009. Hospitals were ranked based on procedure volume. We determined the risk-adjusted mortality, major complication rate, and “failure to rescue” rate (mortality in patients with a major complication) for each tertile. Univariate and multivariate associations were then compared.

Results: We identified 36,624 patients. The mortality rate for the cohort was 1.6%. The major complication rate was 20.4% at low-volume, 23.4% at intermediate volume and 24.6% at high-volume hospitals (p< 0.0001). However, the rate of failure to rescue (death after a complication) was markedly higher at low-volume (8.0%) compared to high-volume centers (4.9%) (p< 0.0001). After accounting for patient and hospital characteristics, women treated at low-volume hospitals who experienced a complication were 58% more likely (OR=1.58; 95% CI, 1.18-2.11) to die than patients with a complication at a high-volume facility.

Conclusion: Mortality is lower for ovarian cancer patients treated at high-volume centers. The reduction in mortality is not the result of lower complications rates, but rather high-volume hospitals' ability to rescue patients with complications.
Poster Session I

THE STUDY ON CHARACTERISTICS OF CANCER STEM CELL IN EPITHELIAL OVARIAN CANCER DORMANT CELL GROUP

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Objective: Established xenotransplanted tumor model and sorted the dormant cells from the transplanted tumor by PKH26 dyes labeling technique and flow cytometry to investigate the stem cell characteristic of dormant cells in PKH26hi subset and provided theoretical basis for ovarian cancer.

Methods: PKH26-labeled SKOV3 cells were injected S.C. into female nude mice. 10 nude mice were separately raised for 3 and 6 weeks. The other 10 nude mice were administered by cisplatin treatment. The single-cell suspensions were separately named SKOV3-P and SKOV3-R. CD44 protein expression was evaluated by flow cytometry. Oct-4 and Nestin expression were evaluated by Real-time PCR. To evaluated the clonogenic potential and tumorigenicity.

Results: OCT4 and Nestin were expressed in PKH26hi and PKH26lo subsets from SKOV3-P and SKOV3-R cells were higher than the PKH26hi subset (P < 0.01); OCT4 and Nestin expressions in PKH26hi subset from SKOV3-R cells were higher than that in SKOV3-P cells (P < 0.05); CD44 protein expression in PKH26hi subsets from SKOV3-P and SKOV3-R cells with higher than that in PKH26lo subsets (P < 0.01); Clonogenic potential in PKH26hi subsets from SKOV3-P and SKOV3-R cells was obviously higher than PKH26lo subsets (P < 0.05); The tumorigenic rates of PKH26hi,lo cells from SKOV3-R were higher than SKOV3-P cells (P < 0.05).

Conclusion: The SKOV3-P-PKH26hi and SKOV3-R-PKH26hi subset over expressed stem cells markers, clonogenic potential and tumorigenicity, the latter was higher than the former. It indicated that the dormant PKH26lo cells in tumor before and after chemotherapy were stem-like cells and the characteristic was obvious after treatment.
FOLLICLE STIMULATING HORMONE RECEPTOR-MEDIATED NANOPARTICULE GENE DELIVERY SYSTEM AS EFFECTIVE THERAPEUTIC FOR OVARIAN CARCINOMA

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Background and aims: Most patients with ovarian cancer are diagnosed at advanced stages and have only a 30% 5-year survival rate. The routine treatment for patients with advance-staged disease is a combination of cytoreductive surgery and chemotherapy. However, conventional chemotherapy has inevitable drawbacks because of the side effects from nonspecific bio-distribution of the chemotherapeutic drugs. To solve such problem, we developed follicle-stimulating hormone receptor (FSHR)-targeted short interference RNA (siRNA) expression plasmid delivery system, which could deliver sufficient therapeutic genes into target cancer cells and therefore bring fewer side effects and increase efficacy.

Methods: FSH peptide β 33-55 was conjugated to polyethylenimine (PEI) via a bifunctional polyethylene glycol (PEG) and complexed with anti chemokine c-x-c motif ligand 1 (CXCL1) plasmid DNA (pDNA) to form FSH-PEG-PEI/pDNA polyplexes at various N/P ratios. The cytotoxicity, transfection efficiency and CXCL1 silencing effect were evaluated respectively.

Results: The FSH-PEG-PEI/pDNA polyplexes showed low cytotoxicity, high transfection efficiency and specific CXCL1 gene silencing effect. The 2% FSH-PEG-PEI conjugate complexed with pDNA at N/P ratio of 25 has better physicochemical properties. The therapeutic siRNA expression plasmid uptake by the ovarian carcinoma cells was through a receptor mediated manner.

Conclusion: The FSH-PEG-PEI conjugate can be used as a novel receptor mediated gene delivery system against ovarian carcinomas. This strategy could be extended to a wide range of targeted gene therapeutics against different cancers.
Poster Session I

THE EXPRESSION OF LIPOCALIN2 IN OVARIAN CARCINOMA AND ENDOMETRIOSIS

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Background: We previously reported that lipocalin2 (LCN2), a molecule involved in iron-transport, was up-regulated in endometrial carcinoma, and the over-expression of LCN2 was associated with poor outcome of the patients with that tumor. In addition, we reported that LCN2 enhanced the migration, invasion and survival of endometrial carcinoma cell. In the present study, we examined the expression of LCN2 in ovarian carcinoma and endometriosis.

Materials and methods: Immunohistochemical staining of LCN2 was performed using the formalin fixed, paraffin-embedded tissue specimens of 46 ovarian carcinoma (12 clear cell, 13 endometrioid, 4 mucinous and 17 serous adenocarcinomas) and 7 ovarian endometriosis. Immunoreactivities were evaluated according to the ratio of positive cells in 200 cells and described as a positivity index (PI, full score 100).

Results: The PIs of clear cell carcinoma (CCC) (PI = 63.3) and endometrioid carcinoma (PI = 46.2), which were associated with ovarian endometriosis, were significantly higher than that of serous adenocarcinoma (PI = 4.9) (P < 0.0005 and P < 0.0005, respectively) or mucinous adenocarcinoma (PI = 11.4) (P = 0.007 and P = 0.141, respectively). The expression of LCN2 was also strongly observed in ovarian endometriosis (PI = 47.1).

Conclusions: LCN2 was up-regulated in ovarian carcinoma associated with endometriosis, suggesting LCN2 to be involved in the tumorigenesis of ovarian carcinoma.
Poster Session I

IDENTIFICATION OF A NOVEL LONG NON-CODING RNA INVOLVED IN THE TUMORIGENICITY OF OVARIAN CLEAR CELL CARCINOMA

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Background: Ovarian clear cell carcinoma (CCC) is known to have poor outcome because of its chemoresistance. Therefore, it is crucial to identify novel therapeutic targets. Recently, several long non-coding RNAs (lncRNAs), such as HOTAIR, have been reported to be aberrantly expressed in human cancers. However, lncRNAs involved in the tumorigenicity of ovarian CCC have not been reported yet.

Aim In this study, we attempted to identify novel lncRNAs that are required for the tumorigenicity of CCC.

Methods: Apoptotic cell death was detected using the MEBCYTO Apoptosis Kit (MBL). Cell growth was measured by MTT assay. For subcutaneous xenograft experiments, ovarian CCC JHOC5 cells infected with a lentivirus expressing a shRNA targeting lncRNA were injected stereotactically into 6-week-old nude mice.

Results: We found that knockdown of a novel lncRNA, termed ASBEL (antisense ncRNA in the BTG3 locus), resulted in a marked increase in apoptotic death of JHOC5 cells. Moreover, knockdown of ASBEL significantly repressed the tumorigenicity of JHOC5 cells.

Conclusion: We identified a novel lncRNA, ASBEL, which is required for the tumorigenicity of CCC. Thus, ASBEL may be a promising target for CCC diagnosis and therapy.
Poster Session I

RELATIONSHIP BETWEEN DOWNREGULATED EXPRESSION OF MOLECULAR CHAPERONE MORTALIN AND REVERSAL OF DRUG RESISTANCE IN OVARIAN CARCINOMA CELLS

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Ovarian cancer is the most lethal gynecologic malignancy. Despite aggressive primary therapy and high initial response rates, most women with advanced ovarian cancer ultimately die due to the development of drug resistance. Molecular chaperone Mortalin was elevated in many human tumors and overexpression of Mortalin was sufficient to increase the malignancy of carcinoma cells. In this study, Mortalin in normal and matched tumor tissue samples of ovarian cancer Tissue Microarrays was analyzed by immunohistochemistry. Results showed that there were some relationships between increased expression of Mortalin and malignancy of ovarian cancer. At the same time, the mRNA and protein levels of Mortalin in cisplatin-resistant human ovarian cancer A2780/cis cell line was significantly higher than in human ovarian cancer cell line A2780 through real-time RT-PCR and Western blot. A2780/cis cells transfected with Mortalin siRNA showed significantly decreased cell proliferation than A2780/cis cells as evaluated by MTT and colony formation assays. Flow cytometric assays showed the downregulation of Mortalin effectively increased the apoptosis induced by cisplatin in ovarian carcinoma cells. The invasion potential of A2780/cis cells was inhibited by the downregulation of Mortalin, which was determined by transwell invasion assay. Results of Western blot revealed that PI3K/Akt, Raf/Mek/Erk and MAPK/p38 signal cascade and p53 were involved in the process through which Mortalin mediated induction in tumor resistance. All these results indicated that Mortalin involved in tumorigenesis and drug resistance of ovarian cancer and downregulation of Mortalin could reverse drug resistance, revealed Mortalin as a novel therapeutic target for ovarian carcinoma.
Poster Session I

PRMT5 OVEREXPRESSION AS AN INDEPENDENT MARKER FOR POOR PROGNOSIS IN OVARIAN CARCINOMA PATIENTS

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Objective: PRMT5 is an predominant type-II arginine methyltransferases, it is involved at various steps in the processes of tumor progression. The aim of this study was to examine the role of PRMT5 in epithelial ovarian cancer (EOC).

Materials and methods: A total of 170 patients, including 118 EOCs, 20 borderline ovarian tumors, 20 benign ovarian tumors and 12 normal ovaries were enrolled in the study. PRMT5 and Ki-67 were measured by immunohistochemical (IHC) in tissue sections. The relationships between PRMT5 expression and clinicopathologic characteristics and Ki-67 were evaluated. PRMT5 protein expression level and clinicopathologic characteristics were correlated with overall survival (OS), progression free survival (PFS) by univariate and multivariate analysis.

Results: PRMT5 was frequently overexpressed in EOC (83.1%), was higher than normal ovary, benign and borderline tumor. Its overexpression significantly correlated with poor differentiation, advanced FIGO stage, lymphatic/vascular invasion, presence of residual tumor. PRMT5 expression was also positive correlation with Ki-67 expression (r=0.377, p<0.001). In univariate survival analysis, overexpression of PRMT5 was significantly associated with decreased OS (p=0.001) and PFS (p<0.001). Moreover, overexpression of PRMT5 was an independent prognostic marker for shortened OS (p=0.021, 95% CI=0.042-0.770) and PFS (p=0.027, 95% CI=0.156-0.893) in multivariate Cox regression analysis.

Conclusion: Overexpression of PRMT5 correlates with an aggressive malignant phenotype and may constitute a novel prognostic maker for EOC. It plays a critical role in regulation of the proliferation of EOC. Thus PRMT5 may represent a clinically effective new target for therapy of ovarian cancer.
POSTMENOPAUSAL AFP-PRODUCING OVARIAN TUMORS (APOTS): PATHOLOGICAL REVIEW OF 14 CASES


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Background: The majority of APOTs are comprised of yolk sac tumor (YST) arising in younger females. Although less common, some of postmenopausal APOTs are diagnostically challenging because of their histological variations.

Design: Fourteen patients (55 to 69 years) were staged at FIGO IA to IV. Preoperative serum AFP ranged from 155 to 199,340 ng/ml. Immunohistochemical study was performed using the following antibodies: AFP, HNF-1β, GCP3, SALL4, and OCT4.

Results: The cases were histologically divided into 3 categories: 4 germ cell tumors composed of YSTs, 5 mixed YST and epithelial tumors, and 5 epithelial tumors. These YSTs were characterized by being of the enteric type, and having the endodermal sinus pattern and glandular pattern. Epithelial tumors associated with YST were clear cell adenocarcinoma (CCA), endometrioid adenocarcinoma, endometrioid borderline tumor, and mucinous borderline tumor. Epithelial tumors were composed of CCA, unclassified adenocarcinoma and carcinoma with solid proliferation. Immunohistochemically, AFP-producing components, including YST and epithelial tumor, were also positive for GPC3, SALL4 and HNF-1β, but were negative for OCT4.

Conclusion: Postmenopausal APOTs are histologically variable due to their heterogeneity such as being YST associated with epithelial tumor. Some postmenopausal APOTs, only composed of epithelial tumor, are difficult to detect AFP production based on the histological findings. These components are immunohistochemically positive for SALL4 and GPC3, indicating germ cell differentiation. The determination of germ cell differentiation in them, linked to AFP production, is supposed to be clinically significant in the selection of the chemotherapeutic regimen and the prognosis.
Poster Session I

PRIMARY FALLOPIAN TUBE CARCINOMA: CLINICOPATHOLOGICAL ANALYSIS OF 101 CASES
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Background and aims: Primary fallopian tube carcinoma (PFTC) is a rare tumor. The aim of this study was to evaluate the clinical and pathological features of PFTC and to identify the prognostic factors.

Patients and methods: 101 patients diagnosed with PFTC in Obstetrics and Gynecology Hospital of Fudan University between February 2003 and November 2011 were included. Clinicopathological data were evaluated respectively. Kaplan-Meier curves were generated, and log-rank tests were used to evaluate survival differences.

Results: Median patient age was 57.0 (range 36-83) years, and the median follow-up was 40.6 (range 5-106) months. Patients most frequently presented with vaginal bleeding or discharge (49.5%) and pelvic pain (28.7%). 31 (30.7%) patients were in FIGO stage I, 28 (27.7%) in stage II, 41 (40.6%) in stage III, and 1 (1.0%) in stage IV. The serous type was histologically predominant (91.1%), and most were grade 3 (67.3%). 82 (81.2%) patients were undergone lymphadenectomy during surgery. 89 (88.1%) patients had residual tumor less than 1 cm. 67 (66.3%) received no less than 6 courses of chemotherapy following surgery. The 5-year overall survival rate was 71.8%. The age at diagnosis, FIGO stage, residual tumor, lymphadenectomy, courses of adjuvant chemotherapy and lymph nodes status were found to be significant prognostic factors individually. After multivariate analysis, only FIGO stage and lymphadenectomy were found to be independent, significant factors for survival.

Conclusion: Besides FIGO stage, lymphadenectomy may play an important role in PFTC patients' survival. Further clinical studies should be conducted to help understanding this uncommon malignancy.
Poster Session I

FOXL2 GENE MUTATION IN PATIENTS WITH OVARY GRANULOSA CELL TUMORS FROM SOUTHWEST CHINA

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Objective: To investigate the Forkhead box L2 gene c. 402C→G mutation (FOXL2 c.402C→G) of the ovary granulosa cell tumors (GCTs) in patients from our institution.

Methods: We reviewed 53 GCT cases that underwent operation in our institution between April 2001 and February 2011, and detected the 402C→G mutation in their paraffin blocks by bi-direct sequencing.

Results: A total of 53 cases were examined, including 47 adult cases (44 primary and 3 recurrent) and 6 juvenile GCTs (5 primary and 1 recurrent). Patients with abdominal masses/non-irregular bleeding symptoms were more likely to be in advanced stage than non-masses or irregular bleeding patients (P< 0.05). Adult GCTs carried a higher mutation rate than juvenile cases (34/47 vs 1/6) (P=0.024). There was a mutation difference between non-irregular bleeding group and irregular bleeding cases (18/21 vs 13/23) (P=0.034). And mutation difference were also found between abdominal masses and non-masses symptome patients (13/13 vs 18/31) (P=0.016). However, no mutation difference was found between the tumors less and tumors larger than 10cm after surgery (22/33 vs 9/11) (P=0.567). Also, no mutation difference were found between stage I and advanced-stage adult patients (61.4% vs 100%), nor between initial and recurrence cases (65.3% vs 75%) (P>0.05).

Conclusion: The FOXL2 402C→G mutation is more likely to occur in adult GCTs than in juvenile GCTs. Patients with the irregular bleeding/non-abdominal masses symptoms were more likely to be in early stages than patients with non-irregular bleeding/mass symptomes; and the later are more likely to carry 402C→G mutation.
Poster Session I

THE CLINICAL SIGNIFICANCE OF HUMAN LYSYL-TRNA SYNTHETASE (KRS) IN PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Objective: Lysyl-tRNA synthetase (KRS) is one of the subtypes in Aminoacyl-tRNA synthetases, which is known for a key molecule for immune response. Recently it is suggested that KRS may be associated with cancer metastasis in vitro study. We investigated clinical significance of KRS overexpression in patients with epithelial ovarian carcinoma (EOC) and its functional role on cell migration and proliferation in ovarian carcinoma cell lines.

Materials and methods: KRS expression was evaluated by immunohistochemical analysis in 39 patients with EOC. In vitro experiment was performed with inhibition of KRS by KRS specific siRNA.

Results: High KRS expression in primary tumor correlated with higher incidence of advanced stage \( (P = 0.037) \). KRS was highly expressed in A2780cp-20 and SKOV3ip-1 human ovarian cancer cell lines and inhibition of KRS by its specific siRNA significantly reduced cell migration and induced low expression of matrix metalloproteinase-9. However, KRS specific siRNA did not show anti-proliferative effect on cancer cells and prognosis on survival was not different based on the expression level of KRS in patients with EOC.

Conclusion: The results of our study suggest that KRS may be responsible for tumor invasion and metastasis in patients with EOC.
SILIBININ INHIBITS TUMOR GROWTH THROUGH DOWN-REGULATION OF ERK AND AKT IN VITRO AND IN VIVO IN HUMAN OVARIAN CANCER CELLS
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Anticancer activity of silibinin, a flavonoid, has been demonstrated in various cancer cell types. However, the underlying mechanisms were not elucidated in human ovarian cancer cells. The present study was undertaken to examine the effect of silibinin in vitro and in vivo on tumor growth in human ovarian cancer cells. Silibinin inhibited cell viability in a dose-and time-dependent manner. Silibinin caused an increase in reactive oxygen species (ROS) generation and the silibinin-induced cell death was prevented by the antioxidant N-acetylcysteine (NAC). Western blot analysis showed that silibinin induced ROS-dependent down-regulation of extracellular signal-regulated kinase (ERK) and Akt. Transfection of constitutively active forms of MEK and Akt prevented the silibinin-induced cell death. Oral administration of silibinin in animals with subcutaneous A2780 cells reduced tumor volume. Subsequent tumor tissue analysis showed that silibinin treatment induced a decrease in Ki-67 positive cells, an increase in TUNEL-positive cells, caspase-3 activation, and inhibition of p-ERK and p-Akt. These results indicate that silibinin reduces tumor growth through inhibition of ERK and Akt in human ovarian cancer cells. These data suggest that silibinin may serve as a potential therapeutic agent for human ovarian cancers.
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Poster Session I

EFFECTS OF THIRD-LINE CHEMOTHERAPY FOR WOMEN WITH RECURRENT OVARIAN CANCER WHO RECEIVED PLATINUM/TAXANE REGIMENS AS FIRST-LINE CHEMOTHERAPY

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Aims: At present, it remains unclear whether the third-line chemotherapy has clinical benefit. In this study, we retrospectively evaluated the effect of third-line chemotherapy.

Methods: We reviewed the medical records of 84 women with recurrent epithelial ovarian cancer who received third-line chemotherapy after platinum/taxan regimens as first-line chemotherapy.

Results: Median age of all cases are 57 years old (range: 32-78). Stage and histologic type are (I: 6, II: 3, III: 52, IV: 23) and (serous: 47, clear cell: 17, endometrioid: 11, mucinous: 2 and other: 7). In first recurrence, 44 cases were platinum sensitive and 40 cases were platinum resistant. The response rate (CR+PR) and clinical benefit rate (CBR: CR+PR+SD) in the cases of treatment-free interval from second-line chemotherapy (TFI) for < 3 months, 3-6 months and >6 months are 3.8% (2/52), 0% (0/6), 23% (6/26) and 9.6% (5/52), 50% (3/6), 85% (22/26), respectively. The cases for which TFI ≥3 months had higher CBR than those with TFI < 3 months (78.1% vs 15.4%, p< 0.001). In addition, the median overall survival (OS) from the onset of third-line was longer for TFI ≥3 months than for TFI < 3 months (795 days vs 281 days, p< 0.001). Finally, TFI was an independent significant prognostic factor for OS by univariate (p< 0.001) and multivariate (HR 5.26, p< 0.001) analysis.

Conclusions: TFI from second-line chemotherapy may associate with the survival benefit of third-line chemotherapy.
Poster Session I

SALVAGE CHEMOTHERAPY USING GEMCITABINE FOR TAXANE/PLATINUM-RESISTANT RECURRENT OVARIAN CANCER: A SINGLE INSTITUTIONAL EXPERIENCE


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Background: The purpose of this study was to report on the safety and efficacy of gemcitabine used as salvage chemotherapy for ovarian cancer.

Methods: From January 2002 to October 2011, 27 patients were treated with gemcitabine for platinum-resistant recurrent ovarian cancer. Gemcitabine (800 mg/m2) was given on days 1, 8, and 15 of every 28 days. Their medical records were retrospectively reviewed.

Results: All 27 patients had previously received paclitaxel/carboplatin doublet and had become platinum-resistant. The median number of previous chemotherapy regimens was 2 (range 1-7). A total of 114 cycles of single-agent gemcitabine was administered, with the median number of 3 (range 1-10). No complete responses (CR) were observed. Partial response (PR) was observed in 5 patients (18.5%). Eight patients demonstrated stable disease (SD). Median time of duration of response for 5 responders was 4 months (range 2-6). Median survival time was 15 months. Patients with PR or SD (n=13) showed significantly better survival compared with a group with progressive disease (n=14) (p=0.03, by univariate analysis). In addition, multivariate Cox proportional hazards analysis revealed that responses to gemcitabine were a significant factor for survival (hazard ratio: 0.08, 95% CI: 0.0138 to 0.5614, p=0.01). Cases with hematologic toxicity included 10 patients (37.0%) with grade 3/4 neutropenia, 3 patients (11.1%) with grade 3 thrombocytopenia, and 3 patients (11.1%) with grade 3 anemia. Non-hematologic toxicity was well tolerated.

Conclusion: Gemcitabine (800 mg/m2) used for recurrent ovarian cancer possesses a modest activity and a well tolerated toxicity.
Poster Session I

POU6F1 IS THE TRANSCRIPTION FACTOR THAT MIGHT BE INVOLVED IN CELL PROLIFERATION OF CLEAR CELL ADENOCARCINOMA OF THE OVARY

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Objective: Clear cell adenocarcinoma (CCC) of the ovary often shows resistance to anticancer agents. We investigated new molecules (transcription factor: POU6F1) developing molecular-targeting therapy for CCC of the ovary.

Methods: RT-PCR and Western blotting were performed to confirm the expression of POU6F1 in cell lines derived from human epithelial ovarian carcinoma. Microarray analyses were performed using two ovarian cancer microarray data sets available on the Internet. Immunohistochemical staining was also done to confirm both the expression and the localization of POU6F1 using human ovarian carcinoma tissue specimens. In addition, the gene cluster located downstream of transcription factor POU6F1 was investigated to analyze its role in the proliferation of CCC via the lysophosphatidic acid receptor, a G protein-coupled receptor. Furthermore, RNA interference studies with siRNA were performed to assess the effect of POU6F1 on proliferation of xenograft tumors after injection of CCC cells into nude mice.

Results: Expression of POU6F1 in mRNA and protein was confirmed in epithelial ovarian carcinoma cells. The microarray analyses indicated that POU6F1 expression was significantly greater in CCC. Immunostaining confirmed the nuclear localization of POU6F1 in CCC (100%). Exposure to the siRNA for POU6F1 reduced the expression of lysophosphatidic acid receptors involved in tumor cell proliferation. POU6F1 siRNA dose-dependently suppressed the proliferation of CCC cells, and a similar effect was confirmed for tumors transplanted into nude mice.

Conclusions: We investigated a transcription factor (POU6F1) as a potential new molecular-target for CCC of the ovary.
Poster Session I

HCTR1 AND ITS RELATED MIR-206 INVOLVED IN PLATINUM RESISTANCE IN OVARIAN CANCER CELLS

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Objectives: This study is aimed to investigate roles of hCTR1 (human copper transporter 1) and related miRNA in DDP resistance ovarian carcinoma.

Methods: We over-expressed hCTR1 in ovarian cancer cells by retrovirus transfection and identified it by Real-time PCR and Western Blot analysis. DDP cytotoxicity was determined by MTT assay, and the concentration of intracellular platinum was investigated by ion-coupled plasma mass spectroscopy (ICP-MS). hCTR1 related miRNAs were selected and confirmed in ovarian cancer cell lines and paired DDP resistance cells. Regulatory function of target miRNA to hCTR1 expression was investigated using transfection of miRNA mimics or inhibitor. We identify the function of miRNA for hCTR1 mRNA by Luciferase assay.

Results: hCTR1 over-expressed ovarian cancer cells accumulated more platinum and showed more sensitivity to DDP (P< 0.01). The higher expression of miR-206 and lower expression of hCTR1 were detected in A2780CP cells compared with A2780 cells. Over-expression of miR-206 led to obvious decreased hCTR1 mRNA level and subsequent protein level. Moreover, luciferase assay documented that miR-206 could suppress the transcription of hCTR1 mRNA by matching seed region in the 3'UTR of mRNA. Concentration of intracellular platinum in A2780 cells transfected with miR-206 mimics was decreased. Meanwhile, contrary result was invested in A2780/DDP cells transfected with miR-206 inhibitor.

Conclusion: Over-expressed hCTR1 increases influx of DDP and sensitivity to DDP in ovarian cancer cells. miR-206 may be involved in DDP resistance through hCTR1 in ovarian cancer.
Poster Session I

EPIGENETIC SILENCING OF INVASION-SUPPRESSIVE HOXB4 IN OVARIAN CANCER

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Background: HOX genes are transcription factors which are important in development and adult tissues. We have shown previously that HOXA4 inhibits cell migration and spreading, while enhancing cell-cell adhesion in ovarian cancer cells. We therefore hypothesized that HOXB4, a paralog of HOXA4, might have functions similar or complementary to those of HOXA4.

Methods: Immunohistochemical analysis for HOXB4 was performed on a tissue microarray comprised of 445 cases of ovarian carcinoma. Reverse transcription PCR and Western blot analysis were used to examine the expression of HOXB4 in ovarian cancer cell lines. Small interfering RNA and forced-expression approaches were used to examine the influence of HOXB4 on the phenotype of ovarian cancer cells.

Results: Negative or faint staining of HOXB4 was observed in 55% of ovarian carcinomas. In contrast, strong HOXB4 immunoreactivity was detected in the fimbrial epithelium of the fallopian tube, a putative source of ovarian cancer. To investigate the mechanism by which the expression of HOXB4 is down-regulated, we treated ovarian cancer cell lines with the DNA hypomethylation agent 5-Aza-2'-deoxycytidine. HOXB4 expression was induced in both a concentration- and time-dependent manner. On a functional level, ovarian cancer cell transwell Matrigel invasion was significantly enhanced by HOXB4 down-regulation, and suppressed by HOXB4 overexpression.

Conclusions: Our tissue microarray and in vitro results suggest that epigenetic silencing (e.g. promoter methylation) might contribute to reduced HOXB4 expression in ovarian carcinomas. Decreased expression of HOXB4, which functions as an inhibitor of cell invasiveness, may promote ovarian cancer progression or metastasis.
Poster Session II

COMPLIANCE WITH HPV VACCINE IN SAUDI ARABIA

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Objectives: To determine factors that influence Saudi parent’s acceptance of HPV vaccination.

Background: Cancer of the cervix is uncommon in Saudi Arabia, approximately 150 cases reported annually, but unfortunately presented in advance stage. The majority of the cases proved to be related to HPV infection. Considering Saudi Arabia as a conservative society with low rate of sexually transmitted diseases (STDs), recently the epidemiology has changed with increase STDs. HPV vaccine is freely prescribed in Saudi since 2006 but the acceptance for vaccination is poor in spite of media awareness.

Methods: A cross-sectional study with sample consisting of 600 parents with children aged 12 to 18 of age attending gynecological clinics and primary health clinics at King Khalid university hospital in Riyadh, Saudi Arabia. Survey questions targeted their opinions about HPV infections, cancer of the cervix, HPV vaccine and their acceptance for vaccination as well as the several factors which are related to avoid the HPV infections.

Results: Only 12 parents out of 600 interviewed vaccinated their children (2%), all the vaccinated children belonged to highly educated parents. A history of genital warts and cervical cancer in the family were strong factors for vaccination. 60% were not aware about the relation between HPV infection, genital warts and cancer of the cervix. Fear of subsequent complications was strong factor to avoid vaccination.
Poster Session II

LAPAROSCOPIC OVARIAN SUSPENSION FOR THE PRESERVATION OF OVARIAN FUNCTION IN PREMENOPAUSAL WOMEN RECEIVING PELVIC RADIOTHERAPY

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Background: Transposing the ovaries out of the radiation field is an option for preserving gonadal function in patients receiving pelvic radiation. The ovarian follicles are sensitive to DNA damage from ionizing radiation. Laparoscopic ovarian suspension prior to pelvic radiotherapy is effective in the preservation of ovarian function in premenopausal women. It will have lower postoperative morbidity and will not delay time to initiate treatment in women undergoing radiation to the pelvis for various indications. Performing oophoropexy the radiation exposure to ovaries dose is reduced to 5-10%. In terms of ovarian exposure to radiation in 40 years and younger up to 1-50 cGy there is no harm, but with 500 cGy exposure up to 60% of the follicles could be damaged

Study methods: Prospective cohort study, it also included retrospective data from charts of patients who underwent oophoropexy from September 2005 to September 2011.

Results: Oophoropexy was performed in 13 patients and 11 of them required pelvic radiation treatment for cervical cancer, which was initiated within 2 to 3 weeks of the procedure. One patient did not need radiation treatment. Three out of 12 patients are deceased. Only one patient required ovarian cystectomy for abdominal pain and another had right oophorectomy done at the time of surgery for recurrent disease. Two women complained of postmenopausal symptoms and one required hormonal therapy.

Conclusions: Ovarian transposition did not delay initiation of treatment in these women undergoing radiation to the pelvis. Our data is small and 65% of the women had ovarian function preservation.
Poster Session II

FEASIBILITY OF CONCURRENT CHEMORADIOThERAPY WITH DOCETAXEL AND CISPLATIN IN PATIENTS WITH ADENOCARCINOMA OF THE UTERINE CERVIX

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Background and aims: Specific treatment strategies tailored to adenocarcinoma of the uterine cervix have not emerged. We aimed to evaluate the feasibility and efficacy of the concurrent chemoradiotherapy with docetaxel and cisplatin.

Methods: We retrospectively reviewed the clinical records of patients with cervical adenocarcinoma treated with concurrent chemoradiotherapy with this regimen. Two to three courses of chemotherapy consisted of docetaxel (50-70 mg/m2) and cisplatin (50-75 mg/m2) along with concurrent whole pelvic irradiation (at a dose of 30-55Gy).

Results: Between January 2007 and December 2011 fifteen patients with stage I b1 - IVb diseases received concurrent radiotherapy with this regimen. Nine patients received intra-arterial infusion, whereas six patients received intravenous infusion. Response rate in primary lesion was 100% and clinical CR rate was 63.6%. Grade 3-4 neutropenia and grade 1-2 diarrhea were most common toxicity, but no patients experienced treatment delay or interruption due to toxicity. Median follow up was 26 (range 7-39) months, central recurrence was not observed, and 3 patients had distant metastases.

Conclusion: Concurrent chemoradiotherapy with docetaxel and cisplatin is feasible and tolerable. Further observation is needed to confirm efficacy of this combination therapy.
Poster Session II

CERVICAL NEOPLASIA AND HUMAN PAPILLOMAVIRUS INFECTION IN RIYADH, SAUDI ARABIA

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It is well-documented that human papillomavirus (HPV) DNA and mRNA, particularly that of HPV-16 and HPV-18, were found in over 80% of cervical carcinoma tissues. There never has been any community study of HPV in Saudi Arabia. This study aimed to describe correlation between HPV positivity and cervical changes in this part of the world. We randomly obtained 519 cervical specimens with consent and demographic data from women attending clinics for routine check-up. The specimens were all subjected to Pap smear examination, HPV-DNA detection by PCR with general primers, and HPV genotype determination by reverse-line hybridization with HPV genotype-specific probes. One hundred and sixty four specimens (31.6%) were HPV-DNA positive by PCR, of these 30 showed cytological changes. Sixty four specimens were positive for cytological changes, of these 30 were also HPV-DNA positive. A strong correlation was found between HPV positivity and Pap smear test positivity [p < 0.001, OR (95% C.I.) 2.833 (1.665-4.820)]. Our findings also indicated that hypertension [p=0.012] was also correlated with HPV infection. No other condition in the demographic data was correlated. There was significant association between each of these factors and HPV positivity. It was also found that the majority of positive HPV-DNA cases were among the women who were 25-44 years of age. These results could contribute to the management of HPV infections in Saudi Arabia and should assist health authorities to make proper decisions regarding bivalent or quadrivalent vaccination of women against HPV to reduce the infection and its associated cervical cancer disease.
CHARACTERISTIC OF PAP SMEAR IN SAUDI ARABIA

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Background and aim: Saudi women population is characterized by low incidence of cervical cancer. We have assessed in this research the characteristics of abnormal pap smear in a Saudi population in comparison with normal pap smears.

Methods: 5000 Pap smears are performed annually at King Abdulaziz Medical Citys, Riyadh, Saudi Arabia where the cytology reporting follows the Bethesda II system. We have reviewed all pap smear results that were performed during the years 2007-2009 and 2011. Abnormal smear patients data was reviewed through their computer and paper based files and was compared with 200 normal smears that were selected randomly and were sampled across the study period.

Results: 841/19650 patients with abnormal Pap smear were identified which made its prevalence 4.3%. Abnormal smear patients characterized of being with lower parity and were more likely to use different contraception methods. Abnormal cervical appearance was associated with higher incidence of abnormal cervical smear (p=0.04), particularly when the cervix is easily bleeding on touch (p=0.02) or is identified with erosion (p=0.02). The only positive history that have characterized patients with abnormal smear was "previous history of abnormal Pap smear" (p=0.001).

Squamous cell abnormalities were identified in 767 (91%) patients (ASC-US 65%, ASC-H 6.5%, LSIL 22%, HSIL 5.5% and SCC 1%). Glandular cell abnormalities were identified in 74 (9%) of the patients (AGUS 72% and adenocarcinoma 28%).

Conclusion: Abnormal Pap smear prevalence is significantly low in Saudi Arabia. Overall, there is high incidence of advanced glandular abnormalities.
Poster Session II

PREVALENCE OF HPV IN UTERINE CERVICAL CARCINOMA AMONG UAE WOMEN

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Uterine cervical cancer is the second most common cancer among females in the United Arab Emirates. Human papilloma virus (HPV) has been implicated as an etiologic agent for the development of primary carcinoma of cervix. The current literature did not show any study determining the types of HPV that are associated with cervical carcinoma among UAE nationals. This is the first study determining the types of HPV that associated with cervical carcinoma among UAE national women. One hundred twenty cases were included in this study. We used Real Time PCR, In situ hybridization and immunohistochemical techniques to verify our objectives. Cervical carcinoma is associated with high risk HPV in 84% of cases while 16% of cases show no association with HPV infection. HPV 16 is the most common type that causes cervical carcinoma among UAE national women and was seen in 71% of cervical carcinomas, while HPV 18 was seen in 4% and HPV 31 & others were seen in 9% of cases.
Poster Session II

MAINTENANCE THERAPY WITH CAPECITABINE: UNEXPECTED REMISSION OF ADVANCED CERVICAL CANCER AND WELL TOLERATED REGIMEN. A CASE REPORT

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Cervical cancer continues to be a significant health burden worldwide. Globally, the majority of cancers are locally advanced at diagnosis, hence, radiation remains the most frequently used therapeutical modality, however the prognosis of advanced stages is extremely poor and cure is rare. We present a case of persistent stage IIIb cervical cancer in which the patient remains disease-free about two years after beginning treatment with capacitabine(xeloda) 500mg twice daily every 2 weeks monthly. This is a well tolerated regimen without impairment in quality of life. In rare cases an unexpected complete clinical remission and long-term survival without evidence of disease may be achieved in patients with advanced, recurrent or metastatic cervical cancer treated with multimodal therapy.
Poster Session II

CONCURRENT CHEMO RADIATION WITH WEEKLY GEMCITABINE AND CISPLATIN IN LOCALLY ADVANCED CERVICAL CANCER

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Background: The standard treatment of locally advanced disease, for almost 80 years, was radiotherapy, however, based on several phase III randomized clinical trials in the past decade concurrent treatment with cisplatin based chemotherapy and radiotherapy is the current standard of treatment for this disease. Gemcitabine has very clear and potent radio sensitizing properties in preclinical and clinical trials. So it can utilize concurrently with radiation. 30 Women with untreated invasive squamous-cell carcinoma of the cervix of stage IIB to stage IVA were enrolled in the study from September 2009 to September 2010.

Methods: 60mg/m² gemcitabine followed by 35mg/m² cisplatin on day one of each treatment week concurrent with Radiotherapy was administered to the whole pelvic region in 25-27 fractions for a total of 50-54Gy followed 1 or 2 weeks later by intracavitary Brachy therapy. All patients underwent a complete physical examination including pelvic examination and MRI to determine the response one and three months after treatment. For acute and late radiotherapy toxicity RTOG classification of adverse effects was used.

Results: In these 30 patients completed The mean age was 58.13± 11.83 (29-78) years. Mean tumor size was 5.87±1.65 cm. After 3 months of final treatment 73.3% had complete and 26.7% had partial response. Grade3 anemia was10%, thrombocytopenia grade3 3.3% and leukopenia grade3 10% found during treatment.

Conclusion: Locally advanced cervical cancer is a highly recurrent and lethal cancer among Iranian women. Gemcitabine is one of drug that is used in phase3 trials in the world. According to our good results in stage 2b cervical cancer we suggest further phase 3 clinical trials to evaluate gemcitabine role in advanced cervical cancer.
Poster Session II

RADIATION WITH CISPLATIN OR CARBOPLATIN FOR LOCALLY ADVANCED CERVIX CANCER: THE EXPERIENCE OF A TERTIARY CANCER CENTRE

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Background: Definitive treatment with concurrent cisplatin and radiation is the standard of care for locally advanced cervix cancer. The optimal management of patients with a contraindication to cisplatin has not been established.

Objectives: To review the impact of concurrent chemoradiation in a cohort of patients with locally advanced cervical cancer.

Methods: All patients with locally advanced cervical cancer treated with definitive radiation were entered into a prospective database. Demographics, stage, histology, recurrence and survival were recorded. Pharmacy records were reviewed to determine concurrent chemotherapy use. The primary endpoint was overall survival (OS), and secondary endpoints were disease free survival (DFS) and rates of primary, nodal or distant failure. Univariate and multivariate analyses were performed.

Results: 442 patients were treated from Jan 1996 to Feb 2011. 269 patients received cisplatin, 59 received carboplatin and 114 received no concurrent chemotherapy. OS was significantly improved with use of concurrent cisplatin compared to radiation alone (adjusted HR 0.53, p=0.001), as was DFS and the rate of distant failure. Use of concurrent carboplatin was not associated with any significant benefit compared to radiation alone in terms of OS or DFS on univariate or multivariate analyses.

Conclusions: The results of this audit are consistent with the known significant survival benefit with concurrent cisplatin chemoradiation. However, concurrent carboplatin did not have a statistically significant benefit although there are potential confounding factors in this small cohort. The available evidence in the literature favors the use of non-platinum chemotherapy rather than carboplatin in patients with contraindications to cisplatin.
TARGETED THERAPY IN SECOND LINE TREATMENT OF CERVICAL CANCER

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Background: Dependence on neoadjuvant chemotherapy in treating cervical cancer is huge in India. We are reporting the results of second line treatment by conventional therapy and Bevacizumab in advanced and bulky early-stage cervical cancer treated in neoadjuvant setting.

Methods: Patients with histologically proven primary carcinoma were potentially eligible for this prospective cohort study. The primary endpoint selected was progression-free survival (PFS). Prior chemotherapy was Cisplatin and taxol used in neoadjuvant setting in 3 wks interval for three such. Treatment in second line consisted of methotrexate (200 mg bolus) and cisplatin (80 mg/m²) in first group. Another group got 50 mg/m² of intravenous cisplatin on day 1 with 2500 mg/m oral capecitabine daily in 2 divided doses for 14 consecutive days in 21-day cycles. We used bevacizumab (2 mg/kg), paclitaxel (80 mg/m²), and carboplatin in three cases. Responses were assessed using response evaluation criteria in solid tumors.

Results: From 2007 to 2010, 18 cases, 11 from radically operated (n= 58) and 7 from only radiotherapy group (n=22) suffered relapse and metastatic disease within two years of neoadjuvant therapy. 16 cases were treated in second line; 8 cases had methotrexate, five cases capecitabine and three cases had Bevacizumab. Complete response was noticed in two cases of Bevacizumab group. Methotrexate group median time to progression was 4 months (95% CI - 0.13 to 3.97), with a median overall survival of 5.5 months. Capecitabine group median time to progression was 5.5 months (95% CI- 0.25 to 7.50), with a median overall survival of 7 months. There was not much difference in the toxicity profile amongst groups.

Conclusion: Results of second line chemotherapy in cervical cancer are unsatisfactory. There is need for combining targeted therapy with conventional chemotherapy. However, prohibitive cost is cause of concern for such therapy in India.
Poster Session II

OVERTREATMENT ISSUES WITH SEE-AND-TREAT MANAGEMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA; A REVIEW

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Introduction: Overtreatment with a 'see-and-treat' protocol for cervical lesions may later result in adverse pregnancy outcomes. Advantages of 'see-and-treat' include a single visit, less emotional stress, and low complication rates. We conducted a literature review in order to define under which circumstances a 'see-and-treat' policy, without a prior biopsy confirming HSIL may be justified.

Materials and methods: Pubmed and the Cochrane Library were searched for studies concerning 'see-and-treat'. Studies were analysed by referral cervical smear, colposcopic impression, histological diagnosis, and country of study. Overtreatment was defined as no, or LSIL in definitive histology after see and treat.

Results: We included 20 studies, with 6198 patients undergoing 'see-and-treat'. Overall overtreatment rates varied from 3-83% across studies. In 1553 patients with high grade cytology and a high grade colposcopic impression, overtreatment was 20.1%, while in 2159 patients with a HSIL cytology, and in 3993 patients with a high grade colposcopic impression, overtreatment was 18.9%, and 39.7% respectively. Overtreatment in high- and low/middle-income countries was 31.1% and 52.6%.

Conclusion: In high income countries, a see-and-treat policy is justifiable only in case of a high grade smear, regardless of the subsequent colposcopic impression. In low/middle income countries see-and treat is justifiable if either colposcopy or cervical smear indicates a high grade lesion. Under certain circumstances (when no follow-up is expected at all) even low grade lesions may be treated with see and treat. In all other cases a biopsy is preferable to have a histological diagnosis before deciding on definitive treatment.
Poster Session II

TRABECETDIN PLUS CISPLATIN IN RECURRENT OR METASTATIC CERVICAL CANCER: A PHASE I-II DOSE-FINDING STUDY

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Background: Trabectedin (T) is active against sarcomas, ovarian cancer and other solid neoplasms and has a synergic action with Cisplatin (C). The aim of this study is to evaluate tolerability and safety of TC regimen in patients affected by metastatic or recurrent cervical cancer.

Patients and methods: Eligibility criteria were: age 18-75; recurrent or metastatic cervical carcinoma; ECOG performance status 0-1; life expectancy > 3 months; normal blood parameters, signed informed consent. Trabectedin was administered intravenously over three hours followed by Cisplatin over one hour, every 21 days. Four different schedules were planned, for 3 cycles: Group A: T 0.4 mg/m2 plus C 50 mg/m2; Group B: T 0.4 mg/m2 plus C 75 mg/m2; Group C: T 0.6 mg/m2 plus C 50 mg/m2; Group D: T 0.6 mg/m2 plus C 75 mg/m2.

Results: Twelve patients were recruited. Median age was 52 years (range 24-65); histotype was squamous in 10 (83%) cases and adenocarcinoma in 2 (17%). Thirty-six courses of chemotherapy were performed. No dose-limiting toxic effects were reported. The schedule D was effective in term of response rate (1 stable disease) with acceptable toxicity profile. Among the 3 patients of group D, one grade 3 neutropenia, one grade 2 liver toxicity and one severe nausea and asthenia were recorded. No life-threatening or irreversible toxicity occurred.

Conclusion: Three-weekly Trabectedin 0.6 mg/m2 plus Cisplatin 75 mg/m2 in patients with metastatic or recurrent cervical cancer can be considered safe and feasible. Toxicity profile of combined drugs is comparable to that of single agents.
Poster Session II

NUCLEAR CO-EXPRESSION OF P14ARF AND P16INK4A AS MARKERS OF UTERINE CERVICAL CANCER-DERIVED CELL LINES WITH HPV

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Background and aims: The Papanicolaou test (Pap) has been responsible for a significant reduction of cervical cancer-related morbimortality. Unfortunately sensitivity and specificity of this test are very low. In order to increase its sensitivity and specificity new markers have been studied and incorporated to cytological and histological methods for diagnosis for cervical cancer, such as p16INK4A that has been considered the immunocytochemical marker of choice for detection of HPV related cancers. We considered that p14ARF could be a complementary marker in order to improve the accuracy of cytological diagnosis because it shares its gene locus to p16INK4A.

Methods: We performed a systematic analysis of several putative cervical cancer markers in various cancer cell lines in order to evaluate their specificity in the detection of HPV related malignancy, including p16INK4A and p14ARF, using immunocytochemistry, immunofluorescence and Western blot analyses.

Results: Most markers were non-specific and could not discriminate HPV infected cancer cell lines from other non HPV malignant cells, especially PCNA and Ki67 that have been also regarded as specific markers. In contrast, nuclear co-expression of p16INK4A and p14ARF was observed only in HPV-transformed cancer cell lines. p14ARF was present conspicuously in the nucleoli of cells. Notably, in C-33A cervical cancer cells (HPV negative) also showed p14ARF staining while p16INK4A was absent from the nuclei of these cells.

Conclusions: We conclude that both markers; p16INK4A and p14ARF are complementary and should be evaluated jointly in immunohistochemical staining in order to improve the accuracy of cytological diagnosis of cervical cancer.
THREE CASES OF UNCOMMON CERVICAL CANCERS

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The clinical and prognostic evaluation of cervical tumors other than squamous cell and adenocarcinoma is hampered by the low incidence and scarcity of the clinical/epidemiological studies in these rare tumors. We present three different uncommon histologic variants of cervical cancer in young women.

Case 1: A 41 year old woman with normal smear history presented with post coital bleeding. Examination revealed an endocervical polyp which was removed, the histology revealing rhabdomyosarcoma. Clinical staging and imaging suggested FIGO Stage 1B disease. Due to the rarity of this tumor in this age group and scarcity of available literature, she was treated by radical hysterectomy. There was no clinical disease evident at surgery and the final histology analysis returned showing no residual disease.

Case 2: A 22 year old woman was referred with a 1 year history of post-coital bleeding. On colposcopy there was a large ectropion and changes suggestive of CIN 2-3. Biopsy histology showed an invasive small cell carcinoma of cervix. At EUA there was a 3x3 cm cervical lesion, with clinical staging of FIGO 1B. Due to the known aggressive nature of this tumor, she was treated by radical chemo irradiation.

Case 3: A 30 year old woman was seen in colposcopy following a smear reporting severe dyskaryosis. Colposcopy suggested CIN 3 changes with early invasion but on biopsy she was found to have a poorly differentiated large cell neuroendocrine cervical carcinoma. She underwent radical hysterectomy and six cycles of adjuvant chemotherapy.

Discussion: There is debate regarding multi-modality treatment including sequence, duration, frequency, and type of chemotherapy agent to be used in the treatment. Spreading population-based knowledge of effects of treatment of these uncommon tumors should help clinical decision making and therefore improve prognosis.

Discussion also includes reproductive outcome of affected women.
Poster Session II

HUMAN PAPILLOMAVIRUS (HPV) TESTING IN THE FOLLOW-UP OF LOOP ELECTROSURGICAL EXCISION PROCEDURE (LEEP) FOR CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)

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Introduction: The follow-up of women treated for high-grade CIN (CIN2+) by LEEP is essential for diagnosis of residual/recurrent disease. Cytology and colposcopy have poor sensitivity, mainly because of alteration in the architecture of the cervix.

Objective: To correlate cytology, HPV testing and colposcopy with residual disease 6 months after treatment of CIN2+ by LEEP.

Methods: 64 women referred for colposcopy because of an abnormal Pap smear, positive high risk HPV (hrHPV) DNA test (Hybrid Capture 2, Qiagen) or unhealthy cervix were included. Twenty-six women diagnosed with CIN2+ on biopsy underwent LEEP. Results of Pap, HC2, colposcopy and biopsy were available pre-procedure and at 6 months follow-up.

Results: All women with CIN were positive for hrHPV at baseline; 8/26 were positive at 6 months. Median hrHPV titre decreased significantly from 116 RLU (range 1.13-1819.29) at baseline vs 0.26 (range 0.15-272.28) at 6 months, p=0.001. Residual disease was present in 3 women with positive endocervical margins, all were hrHPV positive, but only one each were detected on Pap smear and colposcopy. Colposcopy was unsatisfactory in 8/26 cases. Table 1

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>Positive Predictive Value % (95% CI)</th>
<th>Negative Predictive Value % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>hrHPV testing</td>
<td>100 (31.0-100)</td>
<td>79.2 (57.3-92.1)</td>
<td>37.5 (10.2-74)</td>
<td>100 (79.1-100)</td>
</tr>
<tr>
<td>Pap smear</td>
<td>33.3 (1.8-87.5)</td>
<td>91.7 (71.5-98.5)</td>
<td>33.3 (1.8-87.5)</td>
<td>91.7 (71.5-98.5)</td>
</tr>
</tbody>
</table>

[Comparison of HPV test and Pap for follow-up]

compares test performance in follow-up.

Conclusion: hrHPV testing is more accurate than conventional methods of follow-up of CIN2+ since it is not affected by architectural changes. The availability of an affordable HPV test will improve follow-up in low resource situations.
HIGH CLINICAL IMPACT OF FDG-PET ON TREATMENT CHOICE IN RECURRENT CERVICAL CANCER

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Background: The superiority of FDG-PET over CT and MRI in detecting recurrent cervical cancer and determining the extent of the disease is well known. However, there is a lack of data concerning the clinical impact of these extra findings. This is a prospective clinical study investigating the impact of FDG-PET findings on the treatment plans in recurrent cervical cancer.

Materials and methods: 36 patients with suspected recurrent cervical cancer underwent FDG-PET. The clinical impact of FDG-PET results was assessed using the Australian 4-grade scale; high, medium, low or no clinical impact (ref. Fulham Gynecol Oncol 2009). Median follow-up time after FDG-PET was 33 (5-83) months.

Results: FDG-PET was negative in 9/36 patients, all remain relapse-free and alive after a median follow-up time of 61 (55-74) months.

FDG-PET was positive in 27/36 patients. Relapses were histologically confirmed in 26/27 PET+ cases and in 1 case a primary lung cancer was found.

In 58% of the PET+ patients previously unknown sites of metastases were detected. The clinical impact of the FDG-PET results was rated as high in 35%, medium in 23%, low in 42% and none in 4% of the relapsing patients. Intentions of treatment were changed in 30 %, in all but one patient from curative to palliative. Median OS for PET+ patients was 30 (5-83) months.

Conclusions: FDG-PET provided clinically valuable information, with effect on treatment decisions in 15 out of 26 patients. A higher accuracy in the choice of individual treatment level can thus be provided.
IMMUNOCHEMICAL DEFINITION BY CYTOACTIV® OF HUMAN PAPILLOMA VIRUS (HPV)

V.N. Bogatyrev¹,², I.U. Lepina¹, V.V. Popov¹, L.S. Anisova¹, I.V. Panichenko¹, V.V. Shmatkova¹, L. Meyer¹, K.V. Michalev¹

¹N.N.Blokhin Russian Cancer Research Center of Russian Academy of Medical Sciences, Moscow, Russia,
²Nucleon Ltd, Aubonne, Switzerland

The L1 capsid protein is synthesized only during productive infections HPV that results in specific changes in a upper layer of the epithelium which cytologically are diagnosed as a mild and moderate dysplasia (koilocytosis, the increased nucleocytoplasmic ratio).

For data retrospective analysis, 27 patients with complete clinical records were included. The conventional Pap smears and liquid-based slides (Cytospin, Shandon, UK) were immunochemically stained on HPV L1 capsid protein with the help Cytoactiv® (Cytoimmun GmbH, Germany) for screening on all known HPV types, and then were stained with the Cytoactiv® set, which detects L1 capsid protein of high risk HPV (16, 18, 33, 35, 39, 45, 56 types), without application of the special equipment. L1 capsid protein is nuclear protein, therefore only one positively painted nucleus, it is enough to count the slide positive. Staining was performed according to the manufacturer’s protocol. It is possible to use an archival material. Samples can be repeatedly painted. The morphology of a cell remains untouched. At latent infections HPV the L1 capsid protein does not come to light. It comes to light at mild and moderate dysplasia, whereas L1 capsid antigen hardly or is not defined at all high degree intraepithelial neoplasia.

Carried out immunoc hemical research has shown very high prognostic value (over 79%) definitions of productive infection HPV. The technique is easily integrated in existing a cervical cancer screening programs.
Poster Session II

VACCINE AND CERVICAL CANCER SCREEN PROJECT (VACCS) - FIRST RESULTS FROM WESTERN CAPE SITE

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¹Stellenbosch University, Stellenbosch, ²Pretoria University, Pretoria, South Africa

Objectives: VACCS project is a multi centre collaborative study to assess the combination of primary prevention for cervical cancer by HPV vaccination in primary school girls and secondary prevention by screening for the female care-givers.

Methods: Six primary schools in under-privileged areas Cape Town are included in this report. At an information event questionnaires were conducted with the parents or care-givers of female learners, followed by information given to learners and their parents about cervical cancer, screening and vaccination. Learners aged 9 -12 years whose parents gave written consent were subsequently vaccinated using either the licensed bivalent or quadrivalent HPV vaccines. At this study site parents were invited for cervical cytology testing at local health care clinics.

The study was approved by the ethics committee of the University of Stellenbosch. Consent to conduct the study was obtained from the National Departments of Health and Education.

Results: 1246 were eligible for inclusion and consent for vaccination was obtained for 719 girls (57%). 708 Girls received at least one dose at time of analysis. 501 Parents completed a survey assessing knowledge of HPV vaccination and screening. The parent interviews confirmed that this population is reasonably well informed about screening but access to health facilities remains a problem. Knowledge about HPV vaccines was limited but attitudes towards vaccination as health intervention were overwhelmingly positive.

Conclusions: Cervical cancer vaccination is feasible in the South African school system. When a vaccination campaign is combined with cervical cancer screening opportunities the uptake is promising.
Poster Session II

CERVICAL CANCER SCREENING IN A SLUM SETTING USING VISUAL INSPECTION WITH ACETIC ACID: A PILOT STUDY

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¹Massachusetts General Hospital, Boston, MA, USA, ²AK Khan Healthcare Trust, Dhaka, Bangladesh

Introduction: Each year, more than 15,000 Bangladeshi women are diagnosed with cervical cancer, the majority of whom will die from their disease. There are two major challenges facing Bangladesh in regard to the successful prevention of invasive cervical cancer. Firstly, Bangladesh lacks an effective health care delivery infrastructure. Secondly, current strategies employing a screen-and-refer technique face high rates of patient drop out. The current project is a pilot trial targeting the women in the Korail Slum of Dhaka City, Bangladesh, using visual inspection with acetic acid (VIA) with immediate colposcopy and treatment, based on a screen-and-treat approach.

Methods: Laywomen were recruited from the slum to undergo training to perform VIA. Women ages 20-45 were screened. Women with a positive VIA were referred for colposcopy. Those with colposcopic findings of CIN2 or 3 were offered definitive treatment with LEEP at the time of colposcopy.

Results: Forty-four patients underwent screening with VIA. Eight women were VIA-positive, for a screen-positive rate of 18.6%, and underwent colposcopy. Three patients were identified as having probable CIN2-3. One woman underwent a LEEP, successfully performed in the slum clinic. One patient had colposcopic findings concerning for invasive carcinoma and was treated at a nearby hospital where she was diagnosed with a Stage IB1 cervical cancer.

Discussion: Our preliminary results confirm that VIA, as part of a screen-and-treat approach to cervical cancer screening, can be performed safely in a slum setting. Our rates of VIA-positivity are higher than other published results, and warrant further investigation.
Poster Session II

DETECTION OF HPV AND ITS ASSOCIATION WITH DIFFERENT KNOWN RISK FACTORS FOR NEOPLASTIC CERVICAL LESIONS

M.H. Bukhari, K. Saba

King Edward Medical University, Lahore, Pakistan

Objective: Study Rationale was, whether HPV (human papillomavirus) detection may contributes in identification as a major risk factor in cervical neoplastic lesions.

Study design: A cross sectional and Experimental study and Convenience Sampling was performed.

Study settings: 102 cases from Punjab were selected through cervical cytology and histopathology for detection of HPV and its subtype PCR. Data for risk factors were collected by a questionnaire and association of HPV was seen with Positive PCR results. Patient demographics including their age, sexual partners, marital status, socioeconomic, contraceptive and screening history were evaluated to determine whether subsidiary risk factors are associated with HPV and the development of cervical lesions among Pakistani women.

Major outcome: 85% cases of cervical carcinoma were associated with high risk HPV infection

Results: The 46/102 (45%) cases were low grade squamous cell intraepithelial lesions (L-SILs), twenty two (21.5%) cases were high grade squamous cell intraepithelial lesions (H-SILs), 14 cases (13.7%) were squamous cell carcinomas (SCC), 6 (5.8%) cases showed features of adenocarcinoma, ten (9.8%) cases showed cytology of atypical squamous cells of undetermined significance (ASCUS) and 4 (3.9%) cases were of atypical glandular cells of undetermined significance (AGUS). Out of 79 malignant cases 67/79 (85%) were positive for HPV and among them 59/67 (89%) cases were of HPV-16 and 7/67 (11%) cases of HPV-18. Out of 12 cases of adenocarcinoma 5 (41%) showed positivity for HPV-16.

There was strong association of HPV positivity with young age, early marriages, poor socioeconomic condition, abortions, multiparity and smoking but there was no association with multiple marriages.

Conclusion: Frequency of HPV-18 was greater than HPV-16 was detected in cervical neoplastic lesions and was strongly associated with certain known risk factors for cervical carcinoma.
Poster Session II

RESULTS OF COLD KNIFE CONIZATIONS IN BRASILIA’S CENTRAL HOSPITAL IN A 8 YEAR PERIOD - HOW DEEP IS GOOD ENOUGH?

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1 Gynaecologic Oncology, Brasilia Health Department, 2 Gynaecologic Oncology, Hospital de Base do Distrito Federal, Brasilia, Brazil

Objectives: To verify epidemiological and histological data of patients treated with cold knife conization (CKC) for precancerous cervical lesions.

Design: Cross-sectional study of 134 patients between 2001 and 2008. Patients grouped by age, parity, age at sexual initiation, smoking habit and use of oral contraceptive pills. Histological results considered were size (breadth and depth) of the surgical sample, clearance of surgical margins and histological type. Statistically analysis was performed using Fisher’s test (p < 0.05).

Results: An age group dividing line at the age of 50 at the time of CKC treatment was the only statistically significant factor favouring residual disease (positive surgical margins): 31.8% X 12.4% (p = 0.008). We observed similarities between our data and results from other centres regarding the decreasing rate of compromised surgical margins in surgical specimens > 1.6 cm depth (22% X 16.7%) however, this was not statistically relevant (p = 0.293). Multiparity wasn’t a statistically relevant factor for the clearance of margins (23.3% X 10.3%, p = 0.102), as weren’t age at sexual initiation, smoking and use of pills. Punch biopsies showed high sensitivity (98.9%), specificity (87%) and a good positive predictive value (77.2%) for every final diagnosis. Incidence of surgical complications was 21.6%, none severe.

<table>
<thead>
<tr>
<th>Age</th>
<th>Positive margins</th>
<th>Negative margins</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Age &lt; 50</td>
<td>11</td>
<td>12.4</td>
<td>78</td>
</tr>
<tr>
<td>Age &gt;= 50</td>
<td>14</td>
<td>31.8</td>
<td>30</td>
</tr>
<tr>
<td>Totals</td>
<td>25</td>
<td>108</td>
<td>134</td>
</tr>
</tbody>
</table>

p = 0.008

Conclusion: This study reassures the role of CKC in treating precancerous cervical lesions. Final diagnosis were consistent with punch biopsies, providing enough information for safe treatment choices. Patient age at the time of CKC was the only statistically significant risk factor for the clearance of surgical margins.
Poster Session II

THE PLACE OF ANTERIOR PELVIC EXENTERATION IN STAGE IVA CERVICAL CANCER

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¹Clinica Obstetrica-Ginecologie I, University of Medicine and Pharmacy, Târgu-Mures, ²Sf. Constantin Hospital, Brasov, Romania

The main indication for pelvic exenteration is recurrent gynecologic malignancies. The indication for stage IVA cervical cancer and other advanced stages of gynecological cancers are controversial. We present a 57 old patient, in good health condition, with a stage IVA cervical cancer confirmed by IRM and biopsy by cystoscopy, with unilateral uretero-hydrenephrosis. She underwent an anterior pelvic exenteration with urinary non-continent Bricker ileal conduit. The postoperative recovery was uneventful. She was discharged in the 12th postoperative day. The final pathological report showed stage IVA squamous cervical carcinoma with no pelvic lymph nodes metastases. She didn't undergo other adjuvant therapy. Six months after the surgery the patient is disease-free, with a good quality of life. The anterior pelvic exenteration with non-continent Bricker ileal conduit is a feasible surgical technique with a low rate a complications. It could be offered as an alternative for chemoradiation for stage IVA cervical cancer.
Poster Session II

NIMOTUZUMAB IN MAINTENANCE TREATMENT (MT) AND BEYOND DISEASE PROGRESSION (BDP), IN PATIENTS WITH RECURRING OR PERSISTENT CERVICAL CANCER (CC)

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¹Investigación Clínica, Instituto Nacional de Cancerología, Distrito Federal, Mexico, ²Clinical Research, Centro de Inmunología Molecular, Habana, Cuba, ³Clinical Research, Instituto Nacional de Cancerología, Mexico, Distrito Federal, Mexico, ⁴Oncología, Hosp. José López Tabranes, Mtz, Cuba

New treatments modalities resulting in increased progression free survival (PFS) and overall survival (OS) are urgently required in CC. After relapse, the response rate (RR), is limited and the PFS and OS after subsequent salvage treatment regimens steadily decrease, resulting in a median survival of only 3 months after first relapse. Optimal treatment of patients relapsed after 1, 2 or 3 chemotherapy regimens is unknown.

Nimotuzumab (hR3), an EGFR tyrosine Kinase inhibitor, is a potential treatment option in CC

Objective: To evaluate the role of hR3 in MT and BDP in patients with recurring or persistent disease in CC.

Methods: It is an open label, non-comparative, phase II trial, compassionate use as a second, third line or more in patients with CC recurrent or persistent disease. The Treatment consisted of weekly hR3 plus Gemcitabine at a dose 800 mg / m² / SC by 6 cycles and continued with hR3 every 2 weeks in MT or BDP until the patients had unmanageable clinical deterioration or an ECOG greater than 3.

Results: Fifteen patients with CC were recruited, 50% of the patients had 2 or more sites of metastasis and 80% of them > 3 lines of chemotherapy. Median OS was 11 months (range 4 - 17 months), and median PFS was 6 months. The combinations with chemotherapy were safe with low toxicity.

Conclusions: These results suggest that continued hR3 beyond initial PD and MT could play an important role improving OS in patients with CC.
Poster Session II

CYTOLOGY, HPV TESTING AND COLPOSCOPY AS SCREENING METHODS FOR DETECTION OF HIGH GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA IN HIV-INFECTED WOMEN

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1Faculty of Medicine, Chulalongkorn University, 2Thai Red Cross AIDS Research Centre (TRCARC), 3The HIV Netherlands Australia Thailand Research Collaboration (HIVNAT), Bangkok, Thailand, 4Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, 5South East Asia Research Collaboration with Hawaii (SEARCH), Bangkok, Thailand

Background and aims: HIV-infected women are at an increased risk of cervical intraepithelial neoplasia (CIN) and cervical cancer. Screening with cervical cytology is recommended although the low sensitivity is suspected. We studied the diagnostic performances of cytology, HPV testing and colposcopy as screening methods for the detection of high grade CIN in HIV-infected women.

Methods: HIV-infected women were enrolled from the Thai Red Cross Anonymous Clinic. Conventional cytology, HPV testing and colposcopy were performed in all participants at enrollment. Histopathologic findings were used as the gold standard.

Results: Among 275 women enrolled, 11 (4%) had high grade CIN. The sensitivity of cytology, HPV testing and colposcopy to detect high grade CIN were 54.6%, 100% and 81.8%, respectively whereas the specificity were 95.2%, 66.1% and 78.0%, respectively (Table).

<table>
<thead>
<tr>
<th></th>
<th>Cervical cytology</th>
<th>HPV testing</th>
<th>Colposcopy</th>
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</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>54.6%</td>
<td>100%</td>
<td>81.8%</td>
</tr>
<tr>
<td>Specificity</td>
<td>95.2%</td>
<td>66.1%</td>
<td>78.0%</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>30.0%</td>
<td>10.3%</td>
<td>12.2%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>98.2%</td>
<td>100%</td>
<td>99.1%</td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
<td>11.38</td>
<td>2.95</td>
<td>3.73</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.48</td>
<td>0</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Conclusion: HPV testing performed better as a screening method for high grade CIN in women with HIV. Use of low-cost HPV testing should be more widely recommended for high grade CIN screening.
Poster Session II

PREDICTING FACTORS OF PATHOLOGIC SIGNIFICANCE IN WOMEN WITH ATYPICAL GLANDULAR CELLS ON LIQUID-BASED CYTOLOGY

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Background and aims: Atypical glandular cells (AGC) cytology is a diagnostic challenge because it is frequently caused by benign or significant underlying neoplastic conditions. The main outcome considered was the rate and organ origins of significant histopathology of women who had AGC on liquid-based cytology (LBC). Secondary outcome was to determine predicting factors that were associated with the significant diseases.

Methods: The clinical and histological data of AGC women who underwent appropriate investigations from January 2007 to December 2010 were retrospectively reviewed.

Results: A total of 284 women with AGC cytology, mean age was 51.21 years. Overall significant pathology and invasive cancer were 43.3% and 34.5%, respectively, and higher in women with AGC-FN cytology (65.4% and 55.1%) compared with 31.7% and 23.7% of women with AGC-NOS. The serious pathology in AGC women can be predicted by the AGC subtypes, that are AGC-NOS endocervical type (OR, 2.28; 95% CI, 0.79 to 6.55; p, 0.12), AGC-NOS endometrial type (OR, 2.03; 95% CI, 0.69 to 5.93; p, 0.19), AGC-FN endocervical type (OR, 5.64; 95% CI, 1.62 to 19.57; p, 0.006), AGC-FN endometrial type (OR, 4.11; 95% CI, 1.27 to 13.32; p, 0.01), AGC-FN glandular type (OR, 8.23; 95% CI, 2.02 to 33.49; p, 0.003).

Conclusions: The high prevalence of underlying neoplasia in our populations who had AGC cytology was highly clinically significant. The AGC subcategories alone or combined with patients' age can predict significant histopathology for both the frequency and organ sites of neoplasia.
LOSS OF ARID1A/BAF250A EXPRESSION IS RELATED TO SHORTER PROGRESSION-FREE SURVIVAL IN CERVICAL CANCER

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Purpose: This study explored the expression of BAF250a in cervical neoplasias and evaluated its clinical significance and prognostic value.

Materials and methods: Using tissue microarrays (TMA), immunohistochemical staining against BAF250a was performed in cervical tumor materials and matched normal epithelial samples. Staining results were compared with clinical and pathologic features and univariate and multivariate analyses were conducted to explore the prognostic significance of BAF250a expression. For TMA construction, tumor samples from 191 cervical intraepithelial neoplasia (CIN) and 147 cervical cancer patients were used. BAF250a mRNA expression was also evaluated by SYBR Green real-time polymerase chain reaction (PCR).

Results: BAF250a protein expression was lower in cervical cancer and CIN cases compared with normal epithelia (P < 0.001, each), and this decreased expression was significantly associated with increasing tumor stage (P = 0.005), tumor grade (P = 0.029), or tumor size (P = 0.003), and lymph node metastasis (P = 0.020). Loss of BAF250a expression was noted in 27 (18.4%) of 147 cervical cancers. SYBR Green PCR showed low BAF250a mRNA expression in cervical cancer cell lines and tissues. In multivariate analysis, overall survival in cervical cancer patients was significantly shorter in cases with loss of BAF250a expression (HR = 2.78 [1.01-7.63], P = 0.047).

Conclusions: This study shows that loss of BAF250a in cervical cancer is associated with clinicopathologic characteristics and negative prognostic factor. We need to investigate further the role of ARID1A/BAF250a in cervical carcinogenesis.
Poster Session II

SURGERY AND FAILURE OF PRIMARY TREATMENT FOR CERVICAL SMALL CELL NEUROENDOCRINE CARCINOMA: A TAIWANESE GYNECOLOGIC ONCOLOGY GROUP STUDY

T.-C. Chen1, H.-J. Huang2, C.-H. Chen3, Y.-M. Cheng4, K.-J. Yu5, S.-T. Hsu6, G.-J. Wen7, Y.-J. Ou8, Y.-C. Hung9, H.-C. Lai10, C.-M. Ho11, T.-Y. Wang12, T.-C. Chang13

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Objective: Small cell neuroendocrine carcinoma of the uterine cervix (SCNECC) is rare and aggressive. Most patients are diagnosed at early stages whose treatments usually contain surgery. We investigated failure of primary treatment (FPT) and surgery for SCNECC.

Methods: Clinico-pathological archives of 166 patients including FIGO stage I (n=96), II (n=39), III (n=8) and IV (n=23) from 11 hospitals in Taiwan were reviewed.

Results: FPT (n=105) included loco-regional failure (n=31), distant failure (n=42), combining both (n=8), treatment-related death (n=6), and others (n=18). Median time from diagnosis to FPT was 10 months (0-91), and 90% of FPT occurred within 2 years. Survival after FPT did not differ significantly between various salvages, with an overall 3-year rate of 6%. In stage IA IB1 (n=65), the 5-year failure-free survival (FFS) of surgically treated patients (n=63) was 52%. In stage IB2-IIB (n=70), the 5-year FFS of surgically (n=43) and non-surgically (n=27) treated patients were 23% and 61%, respectively (P=0.002). Radiotherapy-containing primary treatment correlated with less loco-regional failure (P=0.000). Primary treatments containing at least 5 cycles of platinum-based chemotherapy (P5+) correlated with better FFS than other chemotherapy-containing treatments (P=0.009) in stage IIB-IV. Overall (n=166), the 5-year FFS by radiotherapy with P5+ (RTP5+) but without surgery (n=19) was 68%, better than 17% by surgery with RTP5+ (n=12; P=0.009) and 35% by other primary treatments (n=135; P=0.038).

Conclusion: For SCNECC, surgery-containing primary treatments link to worse outcome, while non-surgical RTP5+ correlates with significantly better survival. After FPT, successful salvage is rare.
Poster Session II

INFLUENCE OF HPV16 E6/7 ON THE EXPRESSION OF FGF2 AND FGFR TYPE B IN CERVICAL CARCINOGENESIS

Y.-M. Cheng, C.-Y. Chou

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This study investigates the influence of fibroblast growth factor receptor type B (FGFRb) and fibroblast growth factor on cervical carcinogenesis associated with HPV16 E6/7 infection, using primary cancer cells isolated from Taiwanese patients with cervical cancer. Functional interaction between FGFRb in Cx cells and HPV16 E6/7 transfected Cx cells (CxWJ cells) following treatment with FGF-7, according to cell growth, invasive ability, and tumor growth in SCID mice. Our results indicate that the downregulation of FGFRb gene expression in CxWJ cells partially represses proliferation and the invasive ability provided by FGF-7 stimulation. In SCID mice, the FGF2 and FGFR1 gene expression ascend in CxWJ tumor nodule. These data provide evidence of a functional interaction between HPV16 E6/7 in FGFRb and FGF2, suggesting that cooperative stimulation of HPV E6/7 in inactivated FGFRb and the upregulation of FGF2 may be necessary to completely overcome the oncogenic function associated with the progression of cervical carcinogenesis.
Poster Session II

SMALL CELL CARCINOMA OF THE UTERINE CERVIX WITH SIADH (SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE) SECRETION

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Small cell carcinoma (SCC) of the uterine cervix represents an uncommon variant of cervical cancer with an extremely aggressive biologic behavior, minimum survival chances and rapid and fatal clinical course. Neuroendocrine tumors of the uterine cervix are rare and account for approximately 1-2% of all cervical cancer. SIADH has been commonly associated with stage Ib2 small cell carcinoma of lung. SIADH in cervical cancer is even more rare.

A 40 years old woman with stage Ib2 small cell carcinoma of the cervix was treated with radical hysterectomy with pelvic and paraaortic lymph node dissections. Before operation, SIADH was diagnosed on the basis of hyponatremia (120mEq/L), low plasma osmolarity and increased urine specific gravity. The tumor was immunoreactive for neuron-specific enolase (NSE) and chromogranin A (CGA), but not leukocyte common antigen. After operation, pelvic LN metastasis was found and pelvic radiation therapy (ERT) with concurrent cisplatin chemotherapy has been used. This report of the SIADH of the uterine cervix is a relatively rare case in the small cell carcinoma of the cervix presenting with tumor-associated paraneoplastic syndrome.
Poster Session II

'SEE AND TREAT' MANAGEMENT OF HIGH-GRADE ABNORMAL CERVICAL CYTOLOGY IN A RESOURCE-CONSTRAINED AFRICAN SETTING: A RANDOMISED STUDY

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Background: Conventional management of high-grade abnormal cervical cytology requires repeated clinic visits for colposcopic diagnostic and treatment procedures. This is time-consuming, costly and associated with considerable default in follow-up, especially in low-income countries. There is need to examine approaches that will reduce the cost and number of clinic visits without compromising efficiency.

Objective: To compare the treatment outcomes of women with abnormal cervical smears who received immediate Large Loop Excision of Transformation Zone (LLETZ) and those who had directed biopsies prior to subsequent LLETZ.

Method: Women who were referred for abnormal cervical cytology at two centres in southeast Nigeria between August 2009 and December 2011 were examined with the Colposcope. Those with positive colposcopic findings were randomised to receive either immediate LLETZ (2-step group) or directed biopsies (3-step group). Directed biopsy-confirmed cases underwent follow-up LLETZ. Over-treatment, cost, patient compliance, interval between cytology and treatment were compared between the two groups.

Result: A total of 318 women were studied. Over-treatment rate was similar in both groups. Cost per patient and cytology-treatment interval were significantly higher in the 3-step group. Patient compliance was significantly better in the 2-step group.

Conclusion: Immediate 'see and treat' LLETZ for women with high-grade abnormal cervical cytology in southeast Nigeria is cheaper, less time-consuming, associated with better patient compliance and does not lead to significantly higher over-treatment than 3-step management procedure. Immediate 'see and treat' LLETZ may be ideal for management of women with high-grade abnormal cervical cytology in low-resource countries.
Objective: The aim of the study is to investigate the significance of expression rate of human papillomavirus (HPV) L1 capsid protein to predict the low and high-grade cervical intraepithelial neoplasia (CIN) and correlate it with HPV genotype.

Methods: Immunocytochemical staining for HPV L1 capsid protein was carried out on 2,537 samples obtained from women performed liquid-based cytology. Results were compared with histopathology. High-risk HPV DNA was detected by Hybrid capture II (HC-II), and HPV genotypes was performed by HPV DNA chip test. The HPV DNA chip kit contains 24 type-specific probes.

Results: HPV L1 capsid protein was positive in 24.2%(267/1104) of cervicitis, 54.7%(146/267) of CIN I, 54.7%(98/179) of CIN II, 31.7%(239/754) of CIN III, and 6.9%(16/233) of carcinoma. Histopathology diagnosis revealed higher HPV L1 capsid protein expression rate in CIN I, II than CIN III or cancer (p<0.0001). HPV L1 capsid protein and HC-II were positive in 35.1(78/222) of cervicitis, 68.1%(64/94) of CIN I, 60.1%(86/143) of CIN II, 33.1%(229/691) of CIN III, 7.1%(15/210) of carcinoma. Final diagnosis revealed high-risk HC-II and higher HPV L1 capsid protein expression rate in CIN I, II than CIN III or cancer (p<0.0001). HPV L1 capsid protein and HPV 16 were positive in 30.3%(33/109), 48.6%(18/37), 53.1(26/49), 32.6(113/347), and 5.5%(7/127) of cervicitis, CIN I, CIN II, CIN III and cancer, respectively. HPV L1 capsid protein and HPV 18 were positive in 32.7%, 58.3%, 66.7%, 32.6%, 8.8%, respectively.

Conclusions: The expression rate of HPV L1 capsid protein and positive high-risk HC-II in liquid-based cytology specimen was decreased as the histopathology diagnosis severe degree, which may imply the histopathology diagnosis of cervix, predict the progression of cervical lesion, and help to distinguish the cases with CIN I, II and CIN III or cancer.
Poster Session II

LONG-TERM FOLLOW-UP AFTER LOOP ELECTROSURGICAL EXCISION PROCEDURE IN HIGH-GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objective: Loop electrosurgical excision procedure (LEEP) is a basic procedure, conservatively treating high-grade cervical intraepithelial neoplasia (CIN/ II/III).

After LEEP, the close follow-up is essential for an early detection and retreatment of residual and recurrent diseases. The purpose of this study is to evaluate the long-term experience after LEEP and to identify the rate and risk of treatment failure in treating CIN II/III.

Materials and methods: The retrospective review was conducted of 1105 women, who had undergone LEEP and confirmed the final diagnosis of CIN II/III from January, 1999 to December, 2005. Patients were followed with the cervical cytology and colposcopy after initial procedure. If an abnormal cytology was found during a period of follow-up, patients were retreated, and then the diagnosis over CIN was considered as the treatment failure.

Results: The average follow-up period 94.6 months. Overall, 100 patients (9.0%) were detected the treatment failure and the cervical cancer newly developed in nine women (0.8%). 68.0% of treatment failures appeared within 2 years after LEEP, 32.0% beyond 2 years, and 12.0% after 5 years. The treatment failure rates were, 6.2% in the first 2 years, 1.9% between 2 and 5 years, and 1.2% in more than 5 years. Among the various clinicopathologic factors, the surgical margin positivity and cytologic positivity immediately after LEEP were independent risk factors for the treatment failure by using multivariate logistic regression analysis.

Conclusion: LEEP is an effective modality for the treatment of high-grade CIN. But, many patients have a recurrence of disease and development of invasive cancer for a long period of follow-up after initial procedure. Moreover, the surgical margin positivity and cytologic positivity immediately after LEEP lead to the treatment failure. So the constant long-term follow-up should be required to patients, subsequent to the more complete initial excision to high-grade CIN.
POSTER SESSION II

DETECTION OF CANCER CERVIX - IS IT EARLIER NOW?

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Introduction: The state of Tamilnadu, and its capital Chennai has a very high incidence of cancer cervix. The Govt. Hospital for Women and Children, situated in central Chennai, attached to The Institute of Obstetrics and Gynecology, is the biggest tertiary referral hospital for the state of Tamilnadu. Estimating the numbers of women with cancer cervix in the colposcopy clinic in this hospital would be indicative of the current problem of cancer cervix in the state.

Aim: To find out the numbers of women attending colposcopy clinic at the Govt Hospital for Women and Children diagnosed with cancer cervix and to identify the main complaints of the women with early cancer cervix. presenting features at colposcopy.

Materials and methods: The total number of women attending the clinic over a one year study period was 303. In all there were 15 women with early cancer cervix. One woman aged 40 years had adenocarcinoma and all others squamous cell carcinoma. The age group of women with cancer cervix was from 35 to 63 years, with an average age of 49.8 years.

Results and discussion: White discharge was complained of by 60% of women and post menopausal or irregular vaginal bleeding by 80%.

The single most common feature at colposcopy was the presence of abnormal vessels.

Conclusion: The average age at diagnosis was 50 years. The disease trend showed a leaning towards older women and a shift to earlier diagnosis.
Poster Session II

THE EXPRESSION OF ANTIAPOTOTIC PROTEIN API5 IN CERVICAL NEOPLASIAS

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Purpose: It has been shown in various tumors that dysregulation of apoptosis was closely correlated with carcinogenesis and malignant phenotype of tumor cells. The apoptosis inhibitor-5 [API5, also called antiapoptosis clone 11 (AAC11)] is a poorly studied nuclear protein whose expression has been shown to prevent apoptosis after deprivation of growth factor. This study explored expression of API5 and its relationship with the phosphorylated ERK1/2 (p-ERK1/2) in cervical neoplasias.

Materials and methods: Four hundred fifty nine cervical tumor samples and matched normal epithelial samples were arrayed into tissue microarrays. The expression of API5 and p-ERK1/2 was studied using immunohistochemical analysis. The correlation between API5 expression and survival was analyzed using both univariate and multivariate analyses adjusting for the known prognostic factors.

Results: Expressions of API5 was significantly increased in cervical cancer cases compared with normal epitheliums (P < 0.001). Increased API5 expression was observed in patients with increasing tumor grade (P < 0.001) and platinum resistant group. In multivariate analysis, API5 positivity was an independent prognostic factor for disease-free survival (HR = 2.97 [1.24-7.09], P = 0.014) and overall survival (HR = 3.56 [1.22-10.44], P = 0.020).

Conclusions: This study provides evidence for an association between API5 expression and cervical neoplasias and shows that API5 expression predicts poor prognosis in cervical cancer. Our findings also suggest that future research assessing its clinical usefulness would be worthwhile.
Poster Session II

GAMMA-GLUTAMYLTRANSFERASE IS A PROGNOSTIC MARKER IN A PROSPECTIVELY FOLLOWED COHORT OF 113 PATIENTS WITH CERVICAL CANCER

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Background: Gamma-glutamyltransferase (GGT) evidences an emerging risk factor for cancer incidence and mortality.

Aim: The aim of the present study was to investigate the prognostic value of GGT in cervical cancer patients.

Methods: From a prospectively collected cohort of 94,628 healthy Austrian women, we extracted 113 women who developed cervical cancer and for whom at least one GGT measurement prior to diagnosis was available. Cohort data were linked to official Austrian registries to identify deaths.

Results: Serial patterns of longitudinal GGT values significantly differed between the two outcome groups (patients who survived cervical cancer vs. patients who died). Analysis by means of a linear mixed-effects regression models showed significantly lower serial GGT values in the group of cervical cancer survivors (median serial GGT value in patients who survived cervical cancer vs. patients who died: 10 units/L vs 16 units, P < 0.001).

For survival analysis a Cox proportional hazards model with time-varying GGT values was applied in order to accommodate serial GGT measurements per person. In this model GGT was an independent marker for overall survival in the examined cervical cancer patients (P = 0.015, hazard ratio 1.041 per log-unit of GGT, 95% confidence interval 1.008-1.075).

Conclusion: The present study demonstrated a potential clinical usefulness of GGT as a prognostic marker in cervical cancer patients.
Poster Session II

AT THE END OF LIFE: OPTIMIZING QUALITY OF CARE FOR WOMEN DYING OF CERVICAL CANCER

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Objective: To identify characteristics of all gynecologic oncology patients dying in the hospital (IH) and to compare women with cervical cancer dying IH to those dying outside of the hospital (OH).

Methods: Women who died on the gynecologic oncology service from 2000-2009 were identified and demographics, end-of-life quality-of-life (QOL) indicators, and final hospitalization details were abstracted. A sub-analysis was performed comparing women with cervical cancer who died IH to those who died OH.

Results: Seventy-five women died IH on the gynecologic oncology service from 2000-2009. The majority were white (80%) and insured (57%). Fourteen patients received chemotherapy within 14 days of death and 11 died in the ICU. At last admission, 44 women had a “full code” status and 31 had a DNR status. Eighty-six women with cervical cancer died from disease from 2000-2009. Nineteen patients died IH and 7 died in the ICU. Cervical cancer patients dying IH had more hospitalizations during the last 6 month of life (2.8 v. 1.4, P=0.003) and a greater proportion had an ICU stay near death (42% v. 6%, P=0.0001). There was no difference in the use of inpatient palliative care services.

Conclusions: Cervical cancer patients dying IH are more likely to have poor QOL indicators at the end-of-life. The similarity in the use of inpatient palliative care services suggests that end-of-life preparation may begin earlier and in the outpatient setting for women dying OH. Addressing end-of-life care earlier in a woman's disease course may decrease in-hospital mortality and improve QOL for patients.
Poster Session II

WHICH IS BETTER, CDB BY GYNECOLOGIC ONCOLOGIST OR VRB BY GP DETECTING CERVICAL LESIONS, IN SAME CASES AT SAME TIMES?

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Objective: To compare accuracy of colposcopic directed biopsy (CDB) plus ECC by gynecologic oncologist to visual inspection with acetic acid directed cervical biopsy (VDB) in combination with random cervical biopsy (VRB) and endocervical curettage (ECC) by general practice in detecting cervical lesions (HSIL or more) in the same cases at the same times. Is VDB plus VRB plus ECC by general practice can substitute CDB plus ECC by gynecologic oncologist?

Materials and methods: A Wilcoxon sign-rank test, non parametric compare test was carried out on 158 women with abnormal Pap smear at a tertiary care teaching hospital from March, 2011 to June, 2011. The same women with abnormal Pap smears had further investigations such as; VDB and VRB, and CDB plus ECC, and/or loop electrosurgical excision procedure (LEEP). Either VDB plus VRB plus ECC or CDB plus ECC in the same cases at the same time, sometimes LEEP, were used to diagnose cervical lesions. Severest histopathology from any means was taken as the gold standard.

Results: There were 158 patients included in analyses. Detected lesion from CDB plus ECC by gynecologic oncologist not superior to VDB plus VRB plus ECC by general practice

Conclusions: The VDB plus VRB plus ECC can substitute CDB plus ECC in detecting cervical lesions in low-resource settings or in place that has no gynecologic oncologist.
**Poster Session II**

**PATIENTS WITH CERVICAL CANCER; WHY DID SCREENING NOT PREVENT THESE CASES?**

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**Objective:** The aim of this study was to assess the screening history of women diagnosed with cervical cancer in the Nijmegen region, the Netherlands. Additionally, we reviewed all cervical smears assessed as within normal limits (WNL) in the five years preceding the diagnosis of cervical cancer.

**Methods:** Cytological and histological results of 401 women were studied. All women were treated for invasive cervical cancer between 1991 and 2008 at the Radboud University Nijmegen Medical Center. Subsequently, 98 WNL cytological smears within five years preceding the diagnosis cervical cancer were reviewed.

**Results:** Of the 401 women, 269 (67%) women received at least one invitation for the national cervical cancer screening program (NCSP). The remaining 132 women fell outside the target age of the NCSP. One-hundred-and-seven (40%) of the 269 invited women were regularly screened according to the existing guidelines, 95 (35%) irregularly, and 68 (25%) never had a cytological smear (non-responders). Of the 269 invited women, there were 85 (32%) who had one or more normal smears within the last five years preceding the diagnosis cervical cancer. After review, 39% of the smears appeared to be WNL, 18% ASCUS/LSIL, 19% HSIL or more, and 24% was reviewed as unsatisfactory for evaluation.

**Conclusions:** Half of the women with cervical cancer were never screened because of the limited target age range or non-attendance. Twenty-one percent had a normal smear within five years preceding the diagnosis of cervical cancer, caused by interpretation and sampling errors.
Poster Session II

ACCURACY OF INTERNAL EXAMINATION AND ULTRASOUND IN EARLY STAGE NON-BULKY CERVICAL CARCINOMA IN A TERTIARY GOVERNMENT HOSPITAL

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Introduction: Ultrasound is the primary diagnostic tool used by obstetrician-gynecologists in our country. It is widely available, cost-effective, and does not emit ionizing radiation. Transvaginal and transabdominal ultrasound by the obstetrician-gynecologic sonologist is included in the baseline diagnostic work-up of all patients who undergo radical hysterectomy for cervical cancer in our institution in place of CT scan or MRI. Ultrasound is a viable diagnostic tool in a low-resource setting like the Philippines for early cervical cancer where MRI may not be readily available and accessible.

Objective: To determine the accuracy of internal examination and ultrasound in early stage cervical cancer. Specific objectives are to determine the accuracy of internal examination and sonography in measuring tumor size and to determine the accuracy of sonography in detecting vaginal involvement, stromal invasion, parametrial and lymph node involvement by comparing them with the surgicopathologic findings.

Materials and methods: 35 patients diagnosed with early stage cervical cancer for radical hysterectomy with bilateral salpingo-oophorectomy were recruited. Presence of poor prognostic factors was determined by internal examination and sonography and compared with the surgicopathologic result.

Results: Ultrasound and internal examination has an accuracy of 74% and 68% respectively. Ultrasound accuracy in detecting more than one third stromal invasion is 68%, vaginal involvement is 85%, parametrial involvement is 92% and lymph node involvement is 100%.

Conclusion: Ultrasound can recommended as an adjunct to internal examination in the preoperative assessment of early stage cervical cancer.
CLINICO-PATHOLOGICAL AND SURGICAL OUTCOMES ANALYSES OF CERVICAL CANCER PATIENTS TREATED WITH ROBOTIC-ASSISTED RADICAL HYSTERECTOMY

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Objective: To report a single institutional learning curve experience for 5 surgeons performing their first robotic-assisted radical hysterectomies (RARH) for treatment of cervical cancer (CC).

Methods: We retrospectively reviewed medical records from all of the initial 81 CC patients who underwent RARH with pelvic lymphadenectomy (4/1/07 to 12/31/11). Records were analyzed for clinico-pathologic data and operative outcomes, including all complications.

Results: Patients’ mean age was 43.2±13.6 years and BMI 27.8±5.7 kg/m². The FIGO stages were: IB2=6.2%, IB1=75.3%, IA2=17.3%, and IA1=1.2%. Tumor histology was 51.6% squamous, 39.5%, adenocarcinoma, and 8.6% adenosquamous. Mean operative time was 194±40 min, estimated blood loss (EBL) 92±63 mL, and no laparotomy conversions. The transfusion rate was 3.7%. Mean pelvic node count was 20.6±9.1. Infra-mesenteric aortic lymphadectomy was performed in 28.4% of cases (mean 6.0±4.3 nodes). Positive nodes were identified in 16% of cases, all pelvic. Hospital length-of-stay was 1.09±0.43 days. Major complications occurred in 18(22%) cases; one intra-operative ureteral cautery complication required temporary stenting. Five (6%) uretero-vaginal fistula resolved with ureteral catheters and bladder drainage; 3(3.7%) cases required urologic operative repairs. There were no fistula after case #34 following elimination of PK bipolar energy at the vesico-uterine ligament. Other complications included lymphocysts requiring drainage 4(4.9%), cuff dehiscence 1, cuff abscess 1, and cuff bleeding 1.

Conclusions: RARH is an efficient and feasible procedure with low transfusion rate, shorter hospital stay and improved operative measures. Ureter related complications were excessive during the learning curve possibly due to use of bipolar PK forceps near the vesico-uterine ligaments.
Poster Session II

SAFETY AND IMMUNOGENICITY OF THE BI-VALENT VACCINE IN HIV-POSITIVE WOMEN IN SOUTH AFRICA

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Efficacious human papillomavirus (HPV) vaccines can potentially reduce the occurrence of cervical cancer, especially in developing countries where its risk may be increased by the high prevalence of human immunodeficiency virus (HIV) infection.

In a phase I/II study (NCT00586339), asymptomatic HIV-positive women (18-25 years; N=120) were stratified by CD4+ cell count and randomised (1:1) to receive HPV-16/18 vaccine or placebo (Al(OH)₃) (double-blind). HIV-negative subjects (N=30) received HPV-16/18 vaccine (open label). Anti-HPV-16/18 seropositivity rates, geometric mean concentrations (GMCs), CD4+ cell count, HIV viral load, HIV clinical stage, and safety were evaluated.

Regardless of baseline HPV serostatus, 100% of HPV-16/18 vaccinated HIV-positive and HIV-negative subjects were seropositive for HPV-16/18 at Month 2, Month 7 and Month 12. GMCs at each time-point were calculated. In HIV-positive subjects, CD4+ cell count, HIV viral load and HIV clinical stage were unaffected by HPV-16/18 vaccine or placebo administration; no association was found between CD4+ cell count, HIV viral load and magnitude of the immune response. The safety profile was similar between HPV-16/18 vaccinated HIV-positive and HIV-negative subjects, and clinically acceptable for all groups. The HPV-16/18 AS04-adjuvanted vaccine is immunogenic and well tolerated in HIV-infected women.
Poster Session II

URINARY FUNCTION AND EFFECT ON QUALITY OF LIFE RELATED TO TYPE OF TREATMENT IN CERVICAL CANCER: A MULTICENTER OBSERVATIONAL STUDY

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Background:
Given the relatively good prognosis and the age of cervical cancer survivors (CCS), quality of life (QoL) is an aspect of interest in choosing therapies. Urinary problems are a known adverse effect affecting QoL.

Objective: The aim of this study was to evaluate urinary problems and effect on QoL in CCS.

Methods: CCS treated between 2000 and 2010 participated in this multicenter study. Micturition complaints and QoL were assessed using validated self-administered questionnaires (EORTC-CX24, EORTC-C30, Leiden Questionnaire). Three treatment modalities were compared: radical hysterectomy (RHL), surgery plus adjuvant (chemo-)radiotherapy (SART) and primary (chemo-)radiotherapy (PRT). Multivariate analysis was performed to identify factors influencing micturition complaints and QoL.

Results: In total 331 CCS out of 792 invitees responded. Two hundred and five CCS underwent RHL, 62 SART, and 64 PRT. Patients treated with RT (adjuvant or primary) reported significantly more frequency (58% vs. 44%, p 0.003) and incontinence (57% vs. 46%, p 0.011) compared to CCS with RHL. Dysuria was more often reported in the PRT group compared to patients who were treated surgically (29% vs. 13%, p 0.006). Multivariate analysis showed that PRT was significantly associated with frequency and dysuria, parenthood with incontinence.

Compared to the PRT group, more patients who underwent surgery (RHL and SART) reported to feel less/no urge (16% vs. 38%, p < 0.001). The only variables independently affecting QoL were incontinence and PRT.

Conclusion: Treatment of cervical cancer impairs urinary function. Type of treatment defines the character of complaints. Physicians should counsel accurately about these symptoms.
Determining the value of cervical cytology, surgical margin positivity and HPV-DNA testing for determination of residual or recurrent disease in patients undergone LEEP with the diagnosis of CIN II or III.

Material and method: Colposcopy directed biopsy and endocervical curettage applied 77 cases six months after initial LEEP treatment were retrospectively analyzed. Pathologic examination is used in order to determine residual/recurrent disease. Surgical margin positivity at LEEP, cytology after six months, and HPV-DNA PCR test after six months were compared.

Findings and results: In 14 (18.1%) of the 77 cases residual/recurrent disease was determined. HR-HPV was positive in 13 (17%) and negative in 64 (83%). Recurrent/residual disease rate was found to be 12/13 (92%) in HR-HPV positive cases and 2/64 (3%) in HR-HPV negative cases. Out of 25 patients who were surgical margin positive, recurrent/residual disease was determined in 7 (28%). Cytology was positive in 26 (33.8%) cases. Recurrent/residual disease was determined in 2 of the cytology negative and in 12 of the cytology positive cases.

In prediction of residual/recurrent disease, HPV testing (p=0.0001) was found to be superior to surgical margin positivity (p=0.48) or conventional cytology (p=0.001).

Conclusion: HPV test could be used solely for determination of treatment failures after LEEP.
Poster Session II

THE ROLE OF HUMAN PAPILLOMAVIRUS TESTING IN PREDICTING THE RECURRENCE AFTER TREATMENT FOR HIGH-GRADE CERVICAL INTRAEPITHELIAL NEOPLASIA

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Background and aims: To examine the role of high-risk HPV DNA (HR-HPV DNA test) postconisation as prediction of recurrent or residual CIN after treatment of CIN2,3 and to compare this with follow-up cytology and the marginal status of the excised tissue.

Material and methods: 36 women treated with conisation for CIN2,3 were followed by HR-HPV DNA test every 4 months and further followed by colposcopy and cytology for 24 months at 6-month intervals to establish the presence of CIN2,3, proven with colposcopy-directed biopsy occurring within 24 months after treatment.

Results: In 3 of the 36 treated women (8%), residual or recurrent CIN and HR-HPV positive test occurred, 2 had a positive follow-up smear and 1 had positive section margins. From 33 cured women, 7 were HR-HPV positive, 3 had an abnormal smear and 6 had positive section margins. Women with HR-HPV DNA at 4 months showed recurrent or residual CIN in 14% (1/7) if they had normal follow-up Pap smears and in 50% (2/4) if they had abnormal Pap smears. Margin status was not statistically significantly associated with human papillomavirus status.

Conclusions: Persistence or clearance of HR-HPV DNA is an early valid prognostic marker of failure or cure after treatment for CIN2,3 and is more accurate than cytology or section margin status at the time of conisation. The absence of HR-HPV DNA has a 100% negative predictive value.
Poster Session II

THE ROLE OF LYMPHADENECTOMY AND THE SIGNIFICANCE OF THE NUMBER AND STATUS OF LYMPH NODE REMOVED IN CERVICAL CANCER PATIENTS

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Aim: to investigate whether the total number of removed lymph nodes (LNs) and the number of metastatic LNs would prove to be independent prognostic factors for survival in patients with cervical cancer (CC).

Material and methods: Data from patients with CC underwent radical surgery between March 1980 and September 2009 were reviewed. A total of 526 patients were included in the statistical analysis. The total number of examined LNs and their histopathological status were analyzed for their prognostic effect on survival.

Results: Positive pelvic node were found in 102/526 (19%) patients. All of the 8 patients with para-aortic metastases had also pelvic node metastases. At multivariate analysis: vaginal involvement, type of lymphadenectomy and positive nodes all significantly impact negatively on DFS and OS. The log-relative hazard plots of the prognostic effect on DFS and OS of number of positive nodes and total number of nodes removed suggest the existence of a negative association between survival and increasing number of positive nodes, whereas an opposite pattern is shown for increasing number of total nodes removed.

Log-relative hazard plots for OS according to the number of involved lymph nodes (left panel) or the total number of removed lymph nodes (right panel).

[Figure]
Conclusions: Lymph node metastases confer an independent risk for worse survival in patients with CC. Pelvic lymphadenectomy is important for staging and regional disease-control when LNs are involved; however, the extent of lymph node dissection and the overall number of LNs removed do not seem to confer a significant survival advantage, but only a trend is shown.
Poster Session II

PI3KCA MUTATIONAL STATUS AND SURVIVAL IN LOCALLY ADVANCED CERVICAL CANCER (LACC) PATIENTS TREATED WITH CHEMORADIOThERAPY (CRT)

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Introduction: PIK3CA mutational activation is associated with worse outcome in patients with solid tumors, and may predict favorable response to a PI3K/AKT/mTOR pathway inhibitor. However, PIK3CA mutational status has not previously been evaluated in patients with LACC treated with radical CRT.

Objectives:

1. To determine the frequency of PIK3CA mutations in patients with LACC treated with radical CRT.

2. To correlate tumor PIK3CA mutational status in pre-treatment biopsies with overall survival.

Materials and methods: Patients with LACC, treated at a single institution with radical CRT (RT consisting of external beam RT and brachytherapy), with concurrent weekly cisplatin, from 1999-2008, were eligible for this retrospective study. Pre-treatment tumor biopsies (n=157) were retrieved. Genomic DNA was extracted from tumor blocks, and exons 9 and 20 of PIK3CA were analyzed by direct gene sequencing for hotspot mutations.

Results: 82 tumors were successfully sequenced for both exon 9 and exon 20. 19/82 (23%) of tumors were PIK3CA mutation positive; of these, 84% were SCCs. 79% of mutations were in exon 9. PIK3CA mutation positive status was independently associated with worse 5-year overall survival in FIGO I/II patients: 30% vs 85%, [HR 6.3 (95% CI 2.1-19.4), p< 0.05], adjusted for age at diagnosis.

Conclusions: In LACC patients treated with CRT, tumor PIK3CA mutation status was a significant prognostic factor for overall survival. Further evaluation with a larger dataset will be required to validate these findings, and clinical trials will be required to determine whether these patients may benefit from a PI3K/AKT/mTOR pathway inhibitor.
Poster Session II

THE COLPOSCOPIC MANAGEMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA DURING PREGNANCY IN R. MACEDONIA

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Background and aims: Should colposcopy be delayed until 6 weeks postpartum in pregnant patients with atypical squamous cells of undetermined significance (ASC-US) or low-grade squamous intraepithelial lesion (LSIL) cytology according to the incidence of cervical intraepithelial neoplasia (CIN) 2,3 in pregnant patients referred to our university clinic.

Materials and methods: On 312 pregnant women with abnormal cytology, colposcopy was performed at the University Clinic for Gynecology and Obstetrics in Skopje, R. Macedonia.

Results: 312 pregnant patients were identified. The most common cytology was LSIL (40.8%), then ASC-US (32.6%), and HSIL (12.8%). 69 patients (22%) underwent cervical biopsy on their initial colposcopy. 21 had CIN 1, 14 patients had CIN 2, and 11 patients had CIN 3. 22 patients (32%) had no evidence of CIN on biopsy. There were no cases of invasive cervical cancer identified. Of the 234 patients with ASC-US and LSIL cytology, 10 of 39 patients who had a cervical biopsy had CIN 2,3. Of the 128 patients with HSIL, 16 of 30 patients who had a cervical biopsy had CIN 2,3. Repeat colposcopy in the third trimester was performed on 24 patients. Only 1 of 7 patients with a repeat biopsy had CIN 2,3.

Conclusions: Pregnant patients with ASC-US or LSIL cytology rarely have colposcopic findings of CIN 2,3 at their initial colposcopy; therefore, it is reasonable to delay the initial colposcopy in patients with ASC-US and LSIL until 6 weeks postpartum.
Poster Session II

POST-RADICAL Hysterectomy SMALL FIELD RadioTherapy IN SELECTED PATIENTS WITH BULKY FIGO STAGE IB-IIA UTERINE CERVICAL CARCINOMA

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Objective: The aim of this study was to evaluate the radical hysterectomy and post operative small field radiotherapy in stage IB-IIA locally advanced cervical cancer by conducting a 4-year follow-up.

Methods: Between May 2004 and July 2008, 12 locally advanced, stage IB-IIA cervical cancer patients with tumor diameter greater than or equal to 4 cm were treated with radical hysterectomy and pelvic lymphadenectomy followed by post operative local radiotherapy. Patients with high risk tumors received Cisplatin 40mg/m² concurrent with radiotherapy.

Results: We identified 12 patients who fulfilled our eligibility criteria for this study. The mean age at the time of surgery was 41.6 years (range, 37-60 years). The histological cell types included 10 squamous cell carcinomas and 2 adenocarcinomas. Lymphovascular space invasion was found in 6 patients; lateral parametrial invasion, in 2 patients; and vaginal invasion, in 2 patients. In addition, pelvic lymph node metastasis was found in 2 patients. The median follow up time was 36 months.

Conclusions: The findings of this study suggest that adjuvant local radiotherapy (plus chemotherapy in high risk tumors) in selected patients with stage IB-IIA locally advanced cervical cancer after radical hysterectomy and pelvic lymphadenectomy seems to be effective.
Poster Session II

CLINICOPATHOLOGIC FEATURES OF CERVICAL CANCER IN LAGOS UNIVERSITY TEACHING HOSPITAL-LAGOS -NIGERIA

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Background: Cervical cancer is the second most common cause of cancer related morbidity and mortality in women in the developing world.

Objective: To determine the clinical features, risks, stage of the disease at presentation and the histologic type of cervical cancer in Lagos.


Results: 200 cases of cancer of the cervix were seen during the period. The mean age was 58.34 +11.69 years (range 30-88 years). Parity of 83% of patients was > 4. Offensive vaginal discharge was the most common symptom (82.5%), post menopausal bleeding (65%), and post coital bleeding (45.5%). 45% of the sought for healthcare more than 12 months after onset of symptoms. Age at sexual debut was < 18 years in 87%, 77.5% had >2 multiple sexual partners and 85% married before age 20 of years and 77.5% had >4 births).

Only 2.5% of the women ever smoked cigarettes and 7.5% HIV positive

Majority of the patients (92.5%) presented in advanced stages of the disease (stage III to IV). The predominant histologic type was squamous cell carcinoma (90%) followed by adenocarcinoma (6.5%) and adenosquamous in 3.5%.

Conclusion: The clinopathological features of cervical cancer in Lagos are not different from what has been documented in other parts of Africa. Majority of women in Lagos are still presenting in very advanced stage. There is need to increase the awareness and knowledge of this disease.
TEMPORAL TRENDS IN THE RELATIVE SURVIVAL AMONG WOMEN WITH CERVICAL CANCER IN CANADA: A POPULATION-BASED STUDY

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Objective: Cervical cancer is estimated to affect about 1300 women in Canada in 2011 and 350 are expected to die from this disease. We estimated the trends in the relative survival ratio for patients diagnosed with epithelial invasive cervical cancer in Canadian population between 1992-2005.

Methods: A flexible parametric model was used to estimate the relative survival ratio. Relative survival ratio is defined as the observed survival among cancer patients divided by the expected survival in the general population. We incorporated age group, histology of tumour, geographical region, and year of diagnosis into a model to predict two- and five-year relative survival ratio where the effect of each variable was adjusted for the effects of the other variables.

Results: In total 13,424 patients with cervical cancer were included in this analysis. The mean age was 49.3 (SD=16.0) years. Sixty percent of women were younger than 50 years at the time of diagnosis and the relative survival ratio substantially decreased with advancing age. Histology was squamous for 75.4%, glandular for 18.5% and other for 6.2% of cases. This pattern was observed for all regions although with some variation in the proportions. Relative survival improved over time. The best survival was observed for glandular cancers and the worst for other. A higher relative survival ratio was observed for Ontario and British Colombia when compared to the other regions in Canada.

Conclusions: This is the first report that compares relative survival ratio for cervical cancer among geographic regions of Canada. The relative survival decreased with advancing age and showed geographical variations. This work indicates that advances in screening and/or management of women has led to improved relative survival ratios for those with cervical cancer.
Poster Session II

CERVICAL CANCER AWARENESS WEEK IN ONTARIO, CANADA

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Background: The Canadian Women's Federation began a national cervical cancer (CC) awareness campaign. During CC month (October), there was public education and practitioners provide more opportunities for women to receive a Pap test.

Objectives: To determine 1) if there was a change in the Pap test volume; and 2) if the Pap test volume increased, to define the populations affected.

Methods: Pap test rates were determined using a provincial private lab database. The populations of interest were defined by age and as those who did or did not have a Pap test in the prior 3 years.

Results: In women 20-69 year old, during Sep-Nov of each year, the Pap test volume was 409,484 in 2009; 410,139 in 2010 (increase of 0.2%); 413,534 in 2011 (increase of 0.8%). Overall, the rate of Pap tests in Oct (by month or by week) did not appear to change over time; however, there did appear to be a rise in the rate of Pap tests in November. There was a rise in Pap test rates in those age cohorts >20 yrs; this was most marked for those 60-69 yrs. 85.5% of women had had a Pap test within the last 3 years: 15.5% had not had a Pap test within the last 3 year. In those who had had a Pap test in the prior 3 years, the rate of rise in November was 9.5% (2010) and 0.7% (2011). In the group who had not had a Pap test in the prior 3 years, the rate of rise was 12.1% (2010) and 2.9% (2011).

Conclusion: The CC awareness campaign appears to influence test rates in the month after the campaign. The benefit was for those women at greatest risk.
Poster Session II

GEMCITABINE WITH INTENSITY MODULATED RADIATION THERAPY IN RECURRENT CERVICAL SQUAMOUS CELL CARCINOMA - A PILOT STUDY

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Objectives: Cervical carcinoma has a high local failure rate in developing countries with cisplatin based chemoradiation. Most common causes of failure are attributed to presentation at advanced disease, poor performance status, anemia and poor compliance to treatment. A small subset of the patients can be salvaged with Paclitaxel based chemotherapy. We evaluated the feasibility of using prolonged infusion Gemcitabine with Intensity modulated Radiation Therapy (IMRT) in recurrent cancer patients with good performance status.

Methods: 8 patients with recurrent disease (Stage IB and early IIB only) and good performance status were enrolled. All patients had been previously treated with Cisplatin based chemoradiation. At recurrence all patients were treated with prolonged infusion Gemcitabine (1 gm/m² over 8 hours every 14 days). Re-irradiation with IMRT was delivered to a dose of 41.4 - 50.4 Gy / 23 to 28 fractions. All recurrences were more than 12 months after completion of initial RT. 3 patients who had progressive disease but in good KPS were given Pacliaxel - Carboplatin for 6 cycles and then started on IMRT.

Results: All 8 patients were available for evaluation. The main toxicity in this group were non hematological: Vaginal mucositis (Gr 3) - 8/8 (100%), alopecia (Gr 2) - 6/8 (75%), nausea (Gr 2) -6/8 (75%), rash (Gr 3) - 2/8 (25%), dermatitis (Gr 3) - 7/8 (87.5%). Hematological toxicity were: neutropenia (Gr 2) - 3/8 (37.5%), thrombocytopenia (Gr 2) - 4/8 (50%). The overall treatment period ranged from 49 - 62 days (Median 56 days). 1 patient discontinued treatment due to mucositis at 36 Gy and was lost for follow up. Overall response rate was 100 %, CR - 3/8(37.5%) and PR - 5/8 (62.5%). 7 patients had Werthiem´s hysterectomy and are on follow up.

Conclusion: Re-irradiation with IMRT and prolonged infusion Gemcitabine is effective and tolerable.
Poster Session II

PRE-HYSTEROCTOMY CONIZATION IS ABLE TO PREDICT RESPONSE IN LOCALLY ADVANCED CERVICAL CANCER PATIENTS UNDERGONE TO NEOADJUVANT CHEMORADIATION

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Background and aims: To evaluate the histopathological correlation between the cone tissue status and the remaining cervical and paracervical specimens.

Methods: Twenty-eight consecutive FIGO stage IIA2-IIB cervical cancer patients, submitted to neoadjuvant chemoradiotherapy and showing a complete clinical response, were enrolled in this study.

Results: Conization was judged feasible in 22 patients (78.6%). We observed no residual disease in the cone in 18 cases (81.8%), and all these patients showed complete pathological response in the remaining cervical and paracervical tissue. In 3 cones (13.7%) we found a microscopic partial response with negative cervical and paracervical specimen, and in 1 (4.5%) case we observed a macroscopic partial response with a massive vaginal cone’s margin and residual posterior paracervical tumor involvement at definitive diagnosis.

Conclusions: Our study suggests that pathological status of pre-hysterectomy conization could accurately predict pathological response in locally advanced cervical cancer patients submitted to neoadjuvant chemoradiation.
Poster Session II

A PILOT STUDY OF MULTISPECTRAL DIGITAL COLPOSCOPY (MDC) FOR DETECTION OF CLINICAL CERVICAL INTRAEPITHELIAL NEOPLASIA

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Background: Effective and affordable approaches to cervical cancer screening/diagnosis are desperately needed. Current standard of care for developed nations (Pap smear followed by colposcopy and histopathological review where abnormalities are detected) can be time consuming and require multiple visits, resulting in increased expenses. Though HPV vaccines may one day alter approaches to cervical neoplasia screening, the reality is that high demand for screening programs/colposcopic review is still expected for the foreseeable future. Further, use of HPV testing as a screening approach will also lead to increased demand for colposcopy (given the test's relatively low specificity). We have developed a multispectral digital colposcopy (MDC) device that visualizes the entire cervix, aiming to more effectively diagnose disease.

Aim: To evaluate MDC images from patients undergoing loop electrosurgical excision procedure (LEEP) treatment for cervical intraepithelial neoplasia (CIN) against gold standard histopathological findings/colposcopic review, thus assessing whether MDC improves disease detection in vivo.

Results: Complete data from 53 subjects were obtained. MDC examination was able to detect pathology-defined high grade disease (CIN II or III) in most instances (sensitivity, >90%). The observed sensitivity of MDC images was moderate (~55%). Data suggest that the MDC may more accurately delineate disease boundaries than colposcopic review under white light.

Conclusion: CIN is detectable in vivo via MDC, suggesting clinical utility for this device when used in parallel with existing approaches. Our findings provide a strong rationale for larger planned trials that will assess the MDC in concert with a very specific spectroscopic point probe.
INCIDENCE OF LYMPHEDEMA AND BLADDER DYSFUNCTION POST RADICAL HYSTERECTOMY AND PLND- AN IRISH EXPERIENCE

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The aim of the study was to assess the incidence of post-operative lymphedema and bladder dysfunction in women who underwent a radical hysterectomy and pelvic lymph node dissection (PLND) for cervical cancer over a 28 month period (2010-2012).

Women who underwent a radical hysterectomy were contacted by telephone to complete a questionnaire. The National Lymphedema Network (NLN) questionnaire was used. Histology was reviewed to confirm diagnosis and nodal status.

Twenty women completed the questionnaire. Their ages ranged from 28 years to 80 years at the time of surgery. The number of lymph nodes removed at surgery ranged from 10-26. 45% of women had adjuvant radiotherapy (RT), 80% (16/20) were node negative, 40% (8/20) suffered from bilateral lower limb lymphedema, 20% (4/20) from abdominal wall lymphedema, 40% (8/20) had no lymphedema. Of the 60% with lymphedema, 20% were using exercise and massage to treat it, while 10% were using alternative therapies. There was no relationship between presence or site of lymphedema and RT. All women who had greater than 14 lymph nodes removed at surgery had post operative lymphedema. 50% had urinary problems which included urgency, urge incontinence, frequency and incomplete bladder emptying. There was no statistically significant relationship between RT and bladder symptoms. Nineteen women reported their QoL as being very good (4/5) or excellent (5/5) post surgery.

In conclusion radical hysterectomy and PLND is associated with significant morbidity in terms of lymphedema and bladder dysfunction, however it does not have a significant negative effect on QOL.
Poster Session II

LIQUID-BASED CYTOLOGY AND THE DETECTION OF CERVICAL INTRAEPITHELIAL LESIONS IN LOW AND HIGH-RISK WOMEN FOR HPV-RELATED DISEASES

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Background and aims: This is part of the RODEO study designed to evaluate the performance of SurePath™ liquid-based cytology (LBC) running at the Barretos Cancer Hospital.

Methods: Women were randomly assigned to LBC or conventional Pap sampling. All smears were collected in the Prevention Mobile Units (low-risk women) or in the ambulatory of the Barretos Cancer Hospital (high-risk women for HPV related-diseases) from May to December 2010. Regarding the Mobile Units data, 6,001 were assigned to LBC arm and 6,047 to conventional Pap arm.

Results: Considering any cytological abnormality, LBC found 127 cases (2.1%) and conventional Pap test, 61 (1.0%) (P< 0.001). Specific cytological abnormalities have also shown significant differences between the LBC and conventional smears as follows: ASC-US (0.7% vs. 0.1%; P< 0.001); LSIL (0.7% vs. 0.3%; P< 0.001). Despite HSIL cases were twofold more frequent in LBC group than in conventional smears (0.4% vs. 0.2%), no significant difference was found (P=0.186). A larger sample was needed in order to achieve statistical significant difference. In regard of ambulatory data, 2,044 were assigned to LBC and 1,755 to conventional Pap. Cytological abnormality was found in 447 cases (22.1%) in LBC arm and 314 cases (18.1%) in the other arm (P=0.003). Specific cytological abnormality shown significant differences between the LBC and conventional Pap as follows: LSIL (4.9% vs. 2.6%; P< 0.001), HSIL (8.2% vs. 6.2%; P=0.017).

Conclusion: LBC had a better performance in detecting cervical intraepithelial abnormalities in comparison to conventional Pap in high and low risk women for HPV infection.
Poster Session II

QUALITY OF LIFE IN EARLY-STAGE CERVICAL CANCER PATIENTS AFTER RADICAL VAGINAL TRACHELECTOMY VERSUS RADICAL Hysterectomy

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Background: The literature on quality of life (QOL) in patients undergoing radical vaginal trachelectomy (RVT) is scarce. This prospective longitudinal study evaluates QOL after RVT versus after radical abdominal hysterectomy (RAH) and compares the scores with age-matched women from the general population with focus on urological and sexual morbidity.

Methods: Eighteen patients with early stage cervical cancer (CC) operated with RVT and 32 patients operated with RAH were prospectively included. The RVT patients were assessed using validated questionnaires preoperatively, 3, 6 and 12 months postoperatively while RAH patients were assessed once at 12 months post-surgery.

Results: The Global Health Status (GHS) scores improved over time for the RVT group and at 12 months post-surgery mean scores were similar in both groups of patients, but significantly lower compared to healthy women (p= 0.03).

In the RVT group significant problems with lymphoedema, incomplete bladder emptying and decreased bladder sensitivity were observed during the first 3 months post-surgery but improved during the time of observation.

Sexual worry (p= 0.001) and lack of sexual desire (p=0.04) were more frequently reported among patients in both groups compared with controls. Despite of that, sexual activity scores for the RVT group improved significantly during the observation time (p= 0.02).

Conclusion: Patients treated with RVT for early stage CC experience significant problems with lymphoedema, bladder sensory and emptying problems as well as sexual morbidity related to removal of pelvic lymph nodes and most likely injury of the hypogastric plexus. Most symptoms disappeared within 6 months post-surgery.
Poster Session II

PROGNOSTIC FACTORS FOR HIGH-RISK CERVICAL CANCER CASES WITH SQUAMOUS CELL CARCINOMA; COMPARISON BETWEEN RADICAL HYSTERECTOMY WITH AND WITHOUT PARA-AORTIC LYMPHADENECTOMY

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Objective: In curative surgery for cervical cancer, therapeutic significance of para-aortic lymphadenectomy (PALA) has not been evaluated although diagnostic significance was shown. Systematic PALA is not performed routinely and this hampered either large or prospective study on this field. Aim of this study is to investigate significance of PALA in curative surgery for cervical cancer retrospectively.

Methods: 210 cases of cervical cancer with squamous cell carcinoma (SCC) of stage Ib2, IIa2 and IIb were investigated retrospectively, median follow-up period was 59.8 months. Abdominal radical hysterectomy (ARH) with or without PALA was performed at three cancer centers (PALA+: n=91, PALA−; n=119). Prognostic factors for recurrence were investigated by multi-variant analysis. DFS was presented by Kaplan-Meire curve and Log-rank test was applied.

Results: In the cases with pN1, DFS in PALA− group was significantly shorter than that in PALA+ group (Log-rank: p=.023). In PALA- group, DFS of pN1 cases was significantly shorter than that of pN0 cases (Log-rank:p< .001). However, DFS of pN1 was comparable to that of pN0 in PALA+ group (p=.61). Multi-variant analysis revealed that pN1 was a prognostic factor in PALA− group (p < .001) while bulky tumor was the factor in PALA+ group (p = .29). In both groups, bulky tumor cases showed shorter DFS compared with non-bulky tumor cases.

Conclusion: Bulky tumor and pN1 were prognostic factors for recurrence. pN1 was the factor in all cases or PALA− group whereas not the factor in PALA+ group, suggesting that PALA may reduce recurrence rate in pN1 cases.
HIGH RISK (HR) HPV TESTING AS A PRIMARY SCREENING TEST FOR CERVICAL CANCER & PRECANCER IN PERI & POSTMENOPAUSAL WOMEN

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Background: HR HPV is being increasingly used as a primary screening test for cervical cancer & precancer. However, its prevalence varies with age and in different populations.

Aims:

1. To assess HR HPV prevalence & HPV typing in peri & postmenopausal Indian women.

2. To compare HR HPV DNA testing with Pap smear and Visual Inspection with Acetic Acid (VIA) & Lugol's iodine (VILI) as a screening test in this age group, using Colposcopy & directed biopsy as reference standard.

Methods: 405 women, ≥ 40 years were included. Pregnant women & women with history of CIN or cancer were excluded. Cervical scrape for Pap smear & HPV DNA testing was taken. Then, VIA, VILI & Colposcopy was done in all cases. Colposcopic directed biopsies were taken from all screen positive women.

Results: The mean age of the study group was 49.6 years & the mean parity was 3.8. HR HPV DNA was positive in 5.2% women. HPV 16 was predominant, present in 81% of HR HPV positive cases. The sensitivity & specificity of Pap smear, VIA, VILI & HR HPV DNA to detect lesions CIN 2 & worse were 66.7%, 100%, 100%, 88.9% and 93.6%, 62.4%, 67% & 88.1% respectively.

Conclusions: HR HPV testing has the best balance of high sensitivity of 88.9% & high specificity of 88.1%. It has high accuracy of 88.2% & high NPV of 99%. Thus, it is a good screening test for detection of CIN 2 & worse lesions in this age group.
Poster Session II

THE STUDY OF 503 CASES WITH CERVICAL CYTOLOGY INTERPRETED AS ASC-H

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Objective: To explore the risk of CIN II or greater in patients with cytology interpreted as ASC-H.

Method: Patients with ASC-H accepted HPV test, colposcopy-directed biopsy, and endocervical curettage. Surepath was used for cytologic diagnosis. HC II was applied to detect HPV DNA.

Results: 503 patients accepted HPV testing, colposcopy-directed biopsy, and endocervical curettage. 1. The average age was 42.2 years old. 2. 37.3% (188/503) patients were diagnosed CIN II or greater, including 78 cases of CIN II, 103 cases of CIN III, 6 cases of cervical squamous carcinoma, 1 case of cervical adenocarcinoma. There is no cancer be found in women younger than 40 years old. 3. 75.5% (379/503) patients were HPV positive. 4. 48.5% (184/379) were diagnosed CIN II or greater in HPV positive group and 3.2% (4/124) in HPV negative. 5. We divided the patients in 5 groups by age. In patients younger than 30 years old, 30-39 years old, 40-49 years old, 50-59 years old and ≥60 years, the HPV positive rate was 83.6%, 83.4%, 70.3%, 71.4%, 60.5%, respectively. Women who were 60 or older had low HPV positive rate than other groups and the difference was statistic significant. The risk of CIN2 or greater in the five group were 37.3%, 56.6%, 44.4%, 31.7%, 38.5%, respectively.

Conclusions: 1. 37.3% patients with cervical cytology interpreted as ASC-H were diagnosed CIN II or greater and 1.4% were invasive cervical cancer. 2. HPV positive rate was decreased when the patient was older. 3. The negative prospective value of HPV DNA in this study were 96.8%(120/124). 4. HPV DNA test was a helpful tool for cervical cancer screen especially for older than 60.
Poster Session II

PREOPERATIVE PREDICTION OF LYMPH NODE METASTASES WITH SERUM SQUAMOUS CELL CARCINOMA ANTIGEN IN EARLY-STAGE CERVICAL CANCER

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Objectives: Preoperative detection of lymph node metastases in patients with early-stage cervical cancer has the potential benefit of changing treatment options and prevention of multimodality treatment. Aim of this study was to determine the predictive value of preoperative serum squamous cell carcinoma antigen (SCC-Ag) levels for lymph node metastases.

Materials and methods: All patients who underwent a radical hysterectomy with pelvic lymphadenectomy for early-stage (FIGO IB1/IIA) cervical cancer between January 2001 and December 2011 were identified from the Rotterdam Cancer Registry database. SCC-Ag levels were correlated with histopathologic findings. Receiver-operator curves were constructed for SCC-Ag level as a predictor for lymph node metastases.

Results: One hundred fifty-one patients entered the study protocol. Twenty patients (13%) were diagnosed with lymph node metastases. The optimal cut-off for serum SCC-Ag as a predictor of lymph node metastases was 1.0 ng/ml. (sensitivity 65.0%, specificity 83.2%, NPV 94.0%).

Conclusions: Preoperative SCC-Ag levels could predict lymph node metastases in patients with early-stage squamous cell cervical cancer and could be valuable to achieve more tailored diagnostic and treatment strategies.
EVALUATING THE EFFICACY AND SURVIVAL OUTCOME OF NEOADJUVANT CHEMOTHERAPY (NACT) FOLLOWED BY RADIOTHERAPY IN LOCALLY ADVANCED CARCINOMA OF THE CERVIX

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Background: Chemoradiotherapy followed by brachytherapy is the standard treatment for locally advanced cervical cancer. However, a proportion of patients relapse and die of metastatic disease. We investigated the feasibility of introducing NACT with 3-weekly cisplatin (50-70mg/m²)/paclitaxel (175mg/m²) prior to chemoradiotherapy.

Methods: Retrospective data was obtained from records of patients who received NACT for FIGO Stage 1B2 to 4A cervix cancer from December 2007 to December 2010. Inclusion criteria consisted of tumour >5cm and/or bulky pelvic lymphadenopathy, performance status 0-2, and adequate renal function.

Results: 63 patients were identified (median age 47 years). Stage distribution was as follows: stage 1 (4.8%); stage 2 (41.9%); stage 3 (32.2%); and stage 4 (21%). Mean tumour diameter was 6cm (range 3-12cm). The median number of chemotherapy cycles was 4 (range 2-6). Response rate on MRI was >90%. Grade 4 myelosuppression occurred in 1 patient and there was 1 treatment related death. Otherwise chemotherapy was well tolerated. 61 of 63 patients completed subsequent radiotherapy as planned, although only 36 (55%) received concomitant cisplatin. 31 patients (49%) have progressed; 22 (35%) locoregional, 4 (6%) distant, 5 (8%) locoregional and distant. To date, 32 patients (50.8%) are still alive, 6 of them with active disease. 2-year progression free survival is 50% and 2-year overall survival is 60%.

Conclusion: 3-weekly NACT prior to definitive chemoradiotherapy (or radiotherapy alone) leads to a low rate of distant metastases. However, pelvic control is a significant problem in this cohort of patients with very advanced disease.
IMPLEMENTATION OF CERVICAL CANCER SCREENING PROGRAM USING VISUAL INSPECTION WITH ACETIC ACID/LUGOL’S IODINE IN KUTCH DISTRICT, INDIA: A COMMUNITY INITIATIVE

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Background: Visual inspection with acetic acid and Lugol’s iodine (VIA/VILI) is a bridge modality for low resource countries to provide cervical cancer screening until more effective HPV DNA test becomes affordable. Screening programs are often organized by government bodies that may lack trust of the local communities; therefore, such programs suffer from poor participation. Here we aim to describe a locally-sustained VIA/VILI screening program in rural Kutch in India run by KMVS, a local NGO that has partnered with a hospital funded by the Bhojay Sarvodaya Trust.

Methods: All capacity-building measures (funding, community health workers (CHWs), materials) were rooted in the local community. CHWs were sent to national cancer centers for training in screening by VIA/VILI method. Community educational sessions were held prior to screening camps. A three-visit screening model was implemented. At first visit, all women were consented and screened. VIA/VILI positive women returned for biopsy. Biopsy positive women then returned to arrange for treatment.

Results: Screening camps were set up in 28 villages in 2010-2011, screening a total of 1480 married women up to the age of 50. Seven cervical intraepithelial neoplasia positive lesions and 0 invasive cancers were found. None of the women were lost to follow-up.

Conclusions: It is feasible to develop a community level screening program and to provide cancer prevention needs from within a community. Future directions include further evaluation of downstream protocols after VIA/VILI tests, increasing health worker diagnostic and treatment capacity, and determining positive recruitment factors in women attending screening camps.
CERVICAL CANCER ARISING FROM UTERINE DIDELPHYS: REPORT OF THREE CASES AND REVIEW OF THE LITERATURE

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Introduction: Uterus didelphys is the congenital duplication of the uterus caused by the arrested midline fusion of the mullerian ducts. It is mostly asymptomatic and women with a uterus didelphys are generally unaware of the condition. Malignancies arising from this congenital anomaly are very rare.

Case 1: A 53-year-old woman presented to the emergency department with nausea and vomiting. Ultrasonography showed left renal agenesis and two uterine horns with two cervical canals and a 40×36 mm, myoma-like mass between the left uterine horn and the left ovary. Endocervical curettage revealed well differentiated endometrioid adenocarcinoma of the right cervix. She underwent radical abdominal hysterectomy(RAH), bilateral salpingo-oophorectomy(BO) and bilateral regional lymph node dissection (RLND).

Case 2: A 50-year-old woman presented with postcoital bleeding. Pelvic ultrasonography showed a didelphic uterus. Pelvic examination revealed a 4cm cervical mass which was reported as cervical adenocarcinoma after punch biopsy. She underwent RAH+BSO+RLND. Postoperative results were serous adenocarcinoma of the both cervices with invasion of the endometrium and the myometrium, respectively.

Case 3: A 22-year-old woman presented with irregular menstrual bleeding. Ultrasonography revealed a didelphic uterus. Endocervical curettage revealed adenocarcinoma of both cervices. Endometrial biopsy was also reported as mucinous adenocarcinoma metastasis. She underwent RAH+RLND+bilateral ovarian transposition. Pathological evaluation of the surgical materials showed mucinous adenocarcinoma of both cervices with endometrial and myometrial metastasis.

Discussion: Although rare, cervical cancer may be encountered in cases with uterine didelphys. Abnormal cytologic results indicating a high-grade pathology should lead to careful evaluation of both cervices by an experienced colposcopist.
Poster Session II

RARE TUMORS OF THE UTERINE CERVIX: A 5-YEAR EXPERIENCE OF A SINGLE CENTER AND LITERATURE REVIEW

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Aims: To review rare histopathological subtypes of uterine cervical cancer, which were diagnosed and treated gynecological oncology department of in Zekai Tahir Burak Women's Health and Research Hospital in Ankara, Turkey.

Methods: Hospital cancer registry database was reviewed for cervical cancer cases performed between January 2007 and January 2012. Rare histopathological subtypes were identified.

Results: A total of 12 cases of rare cervical tumors were identified during a five-year period. One case had basaloid squamous cell carcinoma, 1 case had embryonal rhabdomyosarcoma, 1 case had myoepithelial carcinoma, 1 case had small cell carcinoma, 2 case had lymphoma, 1 case had malignant mesonephroma, 1 case had adenocarcinoma located in tubulovillous adenoma, 2 cases had neuroendocrine tumors and two cases had verrucous carcinoma.

Conclusions: We presented rare cases of cervical tumors, which all of them were treated with radical abdominal hysterectomy. Treatment choice in these cases are controversial, given the rarity of the tumors. Multicenter collaboration is needed to share experience and to generate treatment algorithms in rare types of cervical cancer.
MESONEPHRIC ADENOCARCINOMA OF THE CERVIX: A CASE REPORT AND REVIEW OF THE LITERATURE

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Introduction: Mesonephric neoplasms derive from mesonephric remnants and are very rarely encountered in the female genital tract. Herein presented is a case of mesonephric adenocarcinoma of the uterine cervix.

Case report: A 48-year-old woman, gravida4 para4 presented with pelvic pain, malodorous vaginal discharge and abnormal vaginal bleeding. On pelvic examination, a 5 cm tumoral mass on the cervix was discovered. There were no signs of parametrial involvement on rectovaginal examination. Biopsy of the tumor revealed a cervical adenocarcinoma. Radical abdominal hysterectomy, bilateral salpingo-oophorectomy and regional lymphadenectomy was performed. After final pathological examination, a mesonephric adenocarcinoma of the cervix was reported. Immunohistochemical analysis showed diffuse staining of the tumor with Cytokeratin and Chromogranin, and focal staining with Vimentin. There was no staining with Inhibin and Calretinin. There were 3 metastatic lymph nodes in the right obturator region. Postoperative course was uneventful. Adjuvant chemoradiation was planned.

Discussion: Mesonephric adenocarcinoma of the cervix is very rarely reported in the literature. These neoplasms exhibit diverse morphological properties and may constitute a diagnostic challenge for pathologists. Surgical treatment or chemoradiation is both acceptable as a primary approach method to these cases. However there are no evidence based data due to the rarity of this neoplasm.
Poster Session II

EFFECTIVENESS OF NURSING INTERVENTIONS TO INCREASE PAP SMEAR TEST SCREENING

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Background: Although Cancer Early Diagnosis and Screening Centers in Turkey offer free comprehensive cervical cancer screening activities, the national standards have not been met, and the reasons woman decline a Pap smear test have not been determined.

Aim: The purpose of this study was to determine the effect of three nursing interventions applied, in succession to the same group of women, to increase participation in Pap smear testing, to increase knowledge and awareness about cervical cancer, and to determine the reason(s) women did not have Pap smear testing.

Methods: A quasi-experimental interventional study conducted in Turkey involved a Pre-intervention stage for pre-testing and three stage-nursing interventions (educational brochures with invitation for Pap smear testing, telephone interviews, and face-to-face interviews) with post-testing.

Results: The target population sample of 2500 women resulted in 510 women (20.4%) having a Pap smear test after receiving the first stage nursing intervention (educational brochure). Second sample of 417 resulted in 158 of 302 eligible women (52.3%) participating. The third sample of 144 resulted in 20 of 54 eligible women (37%) deciding a Pap smear test. A statistically significant difference found between cervical cancer, Pap smear test, and total knowledge scores of women before and after receiving the study's educational brochure.

Conclusion: A three stage nursing intervention was very effective for increasing participation in Pap smear testing. The study confirmed that cervical cancer knowledge, health beliefs, socio-demographic and cultural characteristics are influential factors in Turkish women's decision to participate in Pap smear testing.
POSTER SESSION II

LONG-TERM EVALUATION: THE EFFECT OF CCPDT (CONCURRENT CHEMO-PHOTODYNAMIC THERAPY) IN THE UTERINE CERVICAL AND ENDOMETRIAL CANCER FOR PRESERVING FERTILITY

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CCPDT is a new idea that we made by ourselves. That is, chemotherapy with carboplatin is added in the traditional Photo-Dynamic Therapy (PDT). We have tried this method to treat the uterine cancer. This research is to evaluate the long-term results of CCPDT effect in the uterine cervical and endometrial carcinoma in young women who want to maintain their fertility. Total patients in this study were 5 young nullipara women aged between 27 and 29 who absolutely want to preserve their uterus and cervix. This procedure was initiated by intravenous injection of Photosensitizer. 48 hours before photodynamic therapy and carboplatin (75mg/㎡) was injected 3hours before. Then, Diode laser was applied in the cancer lesion. Screening tests were done during the follow up with interval of 2-3 months in cervical cancer group. Endometrial biopsy and tumor marker (CA 125) were performed at same interval for the patient with endometrial cancer. All patient showed no evidences of recurrence. Follow up period is more then 5 years. And all of them gave a birth through full term vaginal delivery or full term cesarean section. We believe that CCPDT is a painless and safe procedure which can remove pathologic lesion selectively and can preserve uterine and cervical function. For this reason, CCPDT seem to be excellent procedure for nullipara women with cervical cancer or endometrial cancer who want to get pregnant. However the total number of our study was small so more clinical experiences and longer follow up should be needed.
Poster Session II

ANALYSIS OF PREGNANCY OUTCOME AFTER LASER CONIZATION

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Objective: Cervical cancer patients at younger age are increasing rapidly, and those who underwent cervical conization for fertility preservation are also increasing. We retrospectively evaluated pregnancy outcome of patients who underwent LASER conization prior to pregnancy in our institution for the last decade.

Methods: Forty-eight patients were confirmed pregnant after conization, and their pregnancy outcomes were clarified. Their surgical specimens were also re-evaluated.

Results: The average age at conization was 30.2. They included 15 of severe dysplasia, 27 of CIS, 1 of AIS, 3 of Ia1 without lymph-vascular involvement, 2 of Ib1 adenocarcinoma. There were 34(31 cases) term, 9 pre-term and 1 post-term deliveries, 37(34 cases) normal vaginal deliveries, 1 elective Cesarean section and 4 emergency Cesarean sections confirmed. Emergency Cesarean sections included 2 patients after PROM, 2 patients after induction of labor due to post-term pregnancy. There was no statistical significance observed between the volume of surgical specimens and the incidence of pre-term delivery, but the cervical length of a case who resulted in pre-term delivery after pre-term PROM at 29 weeks of gestation was as long as 29mm.

Conclusion: Regardless of our efforts for the upcoming pregnancies, pre-term delivery was observed in 20.5% of the patients who underwent LASER conization in our institution. It seems difficult to predict pregnancy outcomes in the future from conization specimen sizes, and we have to pay close attention to the control of these pregnancies.
Poster Session II

BLOOD TYPE A IS A RISK FACTOR OF LOCOREGIONAL RECURRENCE AFTER DEFINITIVE CONCURRENT CHEMORADIOThERAPY FOR CERVICAL CANCER

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Objective: To identify blood type A as a risk factor of locoregional recurrence after concurrent chemoradiotherapy (CCRT) for cervical cancer.

Materials and Methods: From November 1995 to November 2007, 157 patients with squamous cell carcinoma (SCC) of the uterine cervix were analyzed retrospectively. No patient received PALN irradiation as the initial treatment. All patients received pelvic irradiation and high-dose-rate intracavitary brachytherapy with cisplatin-based chemotherapy. Carcinoembryonic antigen (CEA) and squamous cell carcinoma antigen (SCC-Ag) were measured before and after radiotherapy. We analyzed the actuarial rates of overall survival, locoregional recurrence, and distant metastasis by using Kaplan-Meier curves. Multivariate analyses were carried out with Cox regression models.

Results: Blood type A as an independent factor of locoregional recurrence in patients with pretreatment CEA levels > 5 ng/mL (p = 0.018) but not < 5 ng/mL (p = 0.607). In patients with pretreatment CEA levels ≥5 ng/mL, the 5-year locoregional recurrence rates were 71.4% and 24.9% in type A and non-type A blood group (p = 0.033), respectively. The median time of locoregional recurrence was 23.6 months in patients with both blood type A and pretreatment CEA levels > 5 ng/mL.

Conclusions: High incidence of locoregional recurrence was noted in patients with both blood type A and pretreatment CEA levels > 5 ng/mL. Hysterectomy after CCRT may be considered in patients of this group.
Poster Session II

UROLOGIC COMPLICATION IN LAPAROSCOPIC RADICAL HYSTERECTOMY: META-ANALYSIS OF 20 STUDIES

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Objective: We conducted a meta-analysis to assess between the risk of intraoperative and postoperative urologic complications, and laparoscopic radical hysterectomy (LRH) and lymph node dissection.

Methods: We searched the Pubmed, EMBASE, and Cochrane library for studies published to December, 2011, supplemented by manual searches of relevant bibliographies from the retrieved articles. Two researchers independently extracted the data. Eligible studies had reported perioperative complications and a sample size of at least 10 patients.

Results: The search yield 19 retrospective studies and one prospective cohort study (intraoperative urologic complication, 18 studies; postoperative urologic complication, 16 studies). When all studies were pooled, the odd ratios (OR) of LRH for the risk of intraoperative urologic complications compared to abdominal radical hysterectomy (ARH) was 1.97 [95% confidence interval (CI) 1.23-3.13] and the OR of LRH for postoperative complication risk compared to ARH was 1.35 [95% CI 0.84-2.16]. In subgroup analysis, obesity and laparoscopic type (laparoscopic assisted vaginal radical hysterectomy) were associated with intraoperative urologic complications.

Conclusion: Laparoscopic radical hysterectomy is associated with a significant increased risk of intraoperative urologic complications.
Adenoid basal carcinoma (ABC) of the cervix is a rare condition with preponderence to postmenopausal women. ABC has excellent prognosis so differential diagnosis between ABC and ABC-like lesion of adenosquamous cell carcinoma of the cervix is very important for their different prognosis.

73 years old female visited office due to `high grade significant intraepithelial lesion of cervix´. The colposcopic exam showed a retracted transformation zone in the cervical canal. Cervix punch biopsy revealed CIN 3. She received conization. Pathologic report showed adenoid basal carcinoma (size 2.1 x 1.6cm) and Cervical intraepithelial neoplasia 3 with granular involvement. Deep cervical resection margin was positive with ABC. No definite lymphovascular infiltration or perineural invasion was seen. Computerized tomography revealed no definite mass in cervix and no enlarging pelvic and para-aortic lymph nodes. She received total laparoscopic modified radical hysterectomy and bilateral salpingo oophorectomy, pelvic lymph node dissections. Final pathologic report showed remnant ABC with clear surgical margin and all 23 lymph nodes were negative.
Poster Session II

LAPAROSCOPIC RADICAL TRACHELECTOMY (LRT) WITH ROUND LIGAMENT AND ASCENDING BRANCHES OF UTERINE ARTERY PRESERVATION

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Introduction: The aim of our case report is to describe our experience in laparoscopic radical trachelectomy with round ligament and ascending branches of uterine artery preservation for conservative treatment of early stage cervical cancer.

Case: A 33 years old nulliparous woman had abnormal Pap test. She underwent LEEP and the pathologic result showed adenocarcinoma measuring 0.35 cm. in depth and 0.7 cm. in length. The endocervical and stromal resected margins was not free from adenocarcinoma. After preoperative investigation and counseling for all options of treatment, she decided to undergo laparoscopic radical trachelectomy with bilateral pelvic node dissection. The operative time was 340 minutes.

Estimated blood loss was 700 ml. with no other serious intraoperative complication. The specimen consisted of cervix measuring 3 cm. in length and 2x2 cm. in diameter, anterior and posterior vaginal cuff measuring 1 and 1.5 cm. with the right and left parametrium measuring 3x2.5 cm. Sections showed reactive changes without residual tumor. Fifteen right pelvic lymph nodes and six left pelvic lymph nodes are negative for metastatic tumor. Postoperatively, She had her period on the 9th day after operation and had regular menstruation every month during follow up time. During the 12 months follow-up period, she is well.

Conclusion: To our knowledge this is the first case report of laparoscopic radical trachelectomy with round ligament and ascending branches of uterine artery preservation in South East Asia. Combining with the results in the literatures we believe LRT is feasible and safe for selected cervical cancer patient.
Poster Session II

EZRIN IS AN ENHANCING FACTOR IN CERVICAL CARCINOGENESIS AND PROGRESSION

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Objective: Estrogen regulates ezrin via estrogen receptor. We studied the coincident expression of ezrin and ER's in developing CXCA to evaluate whether there is a failure of ER action or of ER expression during the development of CXCA and ezrin's role in the progression of CXCA.

Material and methods: Individual histological sections from each of 10 patients with one of the following progressively increasing pathological classified cervical lesions (normal, CIN I-III), 7 early invasive CXCA and 10 metastatic CXCA were studied by immunohistochemistry for ERα, ERβ and ezrin. The "H" score was applied for semi-quantitative evaluation of the expression of each protein. Expression of both ER and ezrin were studied in the CXCA cell line (Caski cell) with its cellular location.

Results: The ezrin's was increased progressively parallel to the disease progression reached to the metastatic CXCA. The "H" score of ERβ and ERα underwent a rapid decline by the advent of dysplasia that continued through invasive CXCA. In Caski cell, estrogen intensified immune-reaction of ezrin, induced its redistribution and resulted in cellular phenotypical changes favor to invasion.

Conclusions: Ezrin is overexpressed in CXCA compare with normal cervical tissue and positively correlated with increasing cervical abnormality. Inversely, expression of ERs sharply decreased with disease progression and negatively correlated with CXCA progression. Entire these changes are closely relevant to disease progression and metastasis of CXCA. But this does not explain the ezrin pattern relating ER expression. Further studies are needed to clarify the discordance between ER and ezrin expression.
Poster Session II

A RETROSPECTIVE CLINICOPATHOLOGICAL ANALYSIS OF SMALL CELL CARCINOMA OF UTERINE CERVIX

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Objective: To study the small cell carcinoma of the uterine cervix using the clinicopathological approach and discussing the diagnostic, therapeutic and prognostic aspects of the condition.

Methods: Four cases of bulky (≥4cm) small cell cervical carcinoma in Chinese women are presented in our case study. A retrospective measure is applied to carry out the analysis based on various clinical aspects.

Results: The patients were diagnosed of small cell cervical carcinoma at different stages (Ib1, Ib2, Ila2, IIb based on International Federation of Gynecology and Obstetrics FIGO, 2000) through a sequential hierarchy of physical examinations, blood works, radiological reports, immunohistochemical and pathological tests. Soon after they were diagnosed, different multimodal treatment regimens were chosen for each of the patients. All the patients went through a radical hysterectomy and pelvic lymphadenectomy after which they received different combination of adjuvant chemotherapy. Neoadjuvant chemo was administered in two of the patients. Timely follow-ups were maintained with the patients for the new developments in their condition.

Conclusions: The utmost challenge presented by the disease is the poor prognosis due to its highly aggressive nature, high rate of distant metastases even in an early stage which results the high mortality in the patients. The extreme rarity of the disease (less than 5% of all the malignancies of uterine cervix) also plays a role in hindering adequate research works for the new treatment measures for the disease.
Poster Session II

PREDICTORS OF RESIDUAL DISEASE IN SUBSEQUENT RADICAL HYSERECTOMY SPECIMENS AFTER CONIZATION IN PATIENTS WITH CERVICAL CANCER

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Objective: To correlate findings on conization specimens and other clinical parameters with residual disease in radical hysterectomy specimens in patients with cervical cancer to determine which patients may be eligible for less radical surgery.

Methods: Between 2003 and 2011, 292 patients who underwent radical hysterectomy in our center after conization were included in this retrospective study. The patients who underwent neoadjuvant chemotherapy and/or definitive CCRT and/or radical trachelectomy were excluded.

Results: Mean age of these patients were 54.2 years (28-85). FIGO stage distribution was as followed; 17 patients in IA1, 21 in IA2, 233 in IB1, 10 in IB2 and 11 in others.

In radical hysterectomy specimens, 87 (30%) had no residual cancer, while 205 (70%) had.

Univariate analysis showed that positive resection margin and tumor size more than 2cm were significant factors for predicting residual disease. These factors also significant in a multivariate analysis (positive resection margin OR 6.869, 95% CI 2.734-17.262, p< 0.001; tumor size >2cm OR 2.893, 95% CI 1.638-5.115, p< 0.001).

Positive endocervical and deep margin were significant in predicting residual disease but exocervical margin was not.

The patients with negative resection margin and small tumor (< 2cm) had no residual disease and no recurrence in the median follow-up of 38.6 months.

Conclusion: The resection margin status on conization and clinical tumor size were significant factors for predicting residual cancer in the final radical hysterectomy specimen. Using these factors, we can develop the new guideline about who are eligible for less radical surgery.
Poster Session II

FERTILITY-SPARING MANAGEMENT FOR BULKY CERVICAL CANCER USING NEOADJUVANT TRANS-UTERINE ARTERIAL CHEMOTHERAPY FOLLOWED BY VAGINAL TRACHELECTOMY

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Methods: First, to assess the safety and efficacy of TUAC, survival and pathological complete response data from 39 patients diagnosed with stage Ib2-IIb cervical cancer who participated in 2 consecutive trials during 1997-2006 were analyzed. The neoadjuvant chemotherapy regimens were a combination of TUAC using cisplatin with intravenous nedaplatin or irinotecan. Second, to assess the safety of fertility-sparing management with TUAC, medical records of patients matching the following criteria were reviewed during the same period:

(1) FIGO stage Ib1-IIa;
(2) maximum diameter of tumor, ≥3 cm;
(3) squamous cell carcinoma;
(4) no radiological findings of lymph node metastasis; and
(5) strong patient's desire for preservation of uterus and to undergo TUAC.

Results: The overall 5-year survival rate of the 39 enrolled patients was 81.0% (95% CI, 64.8-93.7%). No malignant cells were found in pathologically examined surgical specimens from 14 patients (35.9%), all of whom were alive without recurrence more than 7 years after treatment. Based on medical records, 7 patients were eligible according to the fertility-sparing criteria, 1 with FIGO stage Ib1 cancer, 5 with stage Ib2, and 1 with stage IIa. One patient with stage Ib1 cancer and 2 with stage Ib2 cancers underwent SVT of paracervical tissues and abdominal lymphadenectomy. Their disease-free intervals were 86, 120, and 65 months, respectively. All 3 had regular menses after surgery but no pregnancies, for personal reasons unrelated to fertility.

Conclusions: Powerful NAC regimens resulted in pathological complete response. Long-term DFI was achieved after fertility-sparing management for bulky cervical cancer in 3 cases.
Poster Session II

PRELIMINARY RESULTS OF THAILAND HUMAN PAPILLOMAVIRUS STUDY: DESIGN, METHOD AND BASELINE DATA

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Background: Limited data on HPV prevalence and genotypic distribution currently exist in Thailand. The cervical cancer screening project 2011 was established for 5,000 Thai females at no costs.

Objective: To determine HPV prevalence and genotype distribution and describe preliminary results of prospective Thailand's cervical cancer screening trial.

Study design: There were 2 phases: a baseline (cross-sectional) phase and a 6-year follow-up (cohort) phase. 6,078 HPV unvaccinated Thai women, aged 20-70 years, were registered. A comprehensive medical, obstetrics and gynecology history, with informed consent, was taken. Pelvic examination and blood testing for antiHIV, HBsAg, VDRL were performed. Liquid-based cytology (Surepath, BD, USA) and HPV testing (Linear array, Roche, USA) were utilized. All women with abnormal cytology or HPV infection underwent colposcopy with biopsy. First round screening would be ended on May 2012.

Results: 3,717 women (mean age 45 years; range 20-70 years) were enrolled in HPV research clinic at Chulabhorn Hospital, Bangkok, Thailand during July 19, 2011-April 3, 2012. Thirty-six were excluded. The prevalence of cytologic abnormalities was 5.7%. High risk (hr)HPV, HPV16, HPV18, HPV6, and HPV11 were detected in 7.1%, 1.4%, 0.5%, 0.3%, and 0.03%, respectively. Positive test for antiHIV, HBsAg, VDRL were 0.2%, 6.9%, 1.7%, respectively. HPV and hrHPV positivity declined with increasing age. The prevalence of cervical intraepithelial neoplasia(CIN) grade1, CIN2 or greater was 3.9% and 1.0%, respectively. Invasive cancer (stageIA1) was found in 4 cases (0.1%).

Conclusion: Preliminary results of HPV study can provide significant prevalence of cytologic abnormalities, hrHPV positivity, and CIN2+ in Thai females.
Poster Session II

PROGNOSTIC SIGNIFICANCE OF POSITIVE PERITONEAL CYTOLOGY IN ADENOCARCINOMA OF THE UTERINE CERVIX

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Objective: A retrospective analysis was carried out to evaluate the prognostic significance of peritoneal cytology in cervical adenocarcinoma.

Methods: The records of 107 patients with FIGO stage IB to IIB cervical adenocarcinoma who underwent hysterectomy were reviewed.

Results: Sixteen patients (15%) had positive peritoneal cytology. The 5-year survival rate among patients with positive or negative cytology was 50% or 87%, respectively, showing a significant difference (log-rank, P < 0.001). The recurrence-free survival (RFS) rate at 36 months in the cytology-positive or -negative group was 53% or 87%, respectively, the difference being significant (log-rank, P=< 0.001). Cox model analysis revealed positive cytology [hazards ratio (HR) 6.27, 95% confidence interval (CI) 2.13-18.41], positive lymph node (HR 6.20, 95% CI 1.87-20.57), ovarian metastasis (HR 5.20, 95% CI 1.18-22.82), and histological grade (HR 5.97, 95% CI 2.00-17.78) to be independent adverse risk factors for survival among the factors analyzed (lymph node status, lymph-vascular space invasion, tumor size, depth in cervical wall, pathological parametrial involvement, infiltration to vagina, ovarian metastasis, and histological grade). Cox model analysis showed that positive cytology (HR 4.58, 95% CI 1.48-14.16), positive lymph node (HR 7.61, 95% CI 2.69-21.54), and histological grade (HR 6.13, 95% CI 2.14-17.77) were independent adverse risk factors for RFS. The incidence of peritoneal spread at the first recurrence among the cytology-positive group (62.5%) was significantly higher than that among the cytology-negative group (12.5%) (Fisher’s exact test, P=0.021).

Conclusion: The presence of positive peritoneal cytology appears to be an independent prognostic risk factor in patients with cervical adenocarcinoma.
Poster Session II

Efficacy of Personalized Peptide Vaccine in Patients with Advanced or Recurrent Cervical Cancer

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Objective: The aim of this study is to evaluate the safety and efficacy of the personalized peptide vaccine (PPV), in patients with advanced or recurrent cervical cancer.

Methods: The candidate peptides for PPV were screened from HLA (HLA-2, A11, A24, A26, A31 or A33) matched peptide by measurement of anti-peptide antibody in the pre-vaccination sera of the patients. Up to 4 peptides showing higher titer of IgG antibody, were given subcutaneously, 6 times the first week, followed by 6 times every 2-week interval. Peptide specific humoral immune response was evaluated by the Luminex method. The primary endpoint was overall survival, and the secondary endpoint was an increase in humoral response against vaccinated peptides and acute toxicity.

Results: Ten patients with cervical cancer have been enrolled in this study so far. Increased IgG titer was observed in 6 of the 10 patients at the 6th vaccination and, in 8 out of 8 at the 12th vaccination. No serious adverse effects have been observed. Median survival time was 512 days.

Conclusion: PPV seems to be feasible and effective with regard to overall survival in advanced or recurrent cervical cancer patients so far. Further investigation, involving a greater number of patients is required.
Poster Session II

ESTABLISHMENT OF A CERVICAL CANCER SCREENING AND TREATMENT PROGRAM IN WESTERN KENYA

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Background: Cervical cancer is a major source of morbidity and mortality in developing nations, particularly among HIV-infected women, a population with higher prevalence and poorer prognosis. In 2010 a nurse-driven “see and treat” strategy using visual inspection with acetic acid (VIA) and cryotherapy was introduced into a large HIV program in Western Kenya, with subsequent expansion from a central clinic to 3 rural outreach clinics. Patients with a positive screen but ineligible for cryotherapy were referred to physicians for colposcopy/LEEP. Patients with cervix cancer were referred to a tertiary hospital-based cancer treatment program.

Results: In 2 years 6,787 women were screened. Monthly screening increased from 149 in June 2010, to 855 in October 2011. 1,331 were screened as positive (19.6%), and 949 (71.3%) of them had HIV. 206 underwent cryotherapy, 754 underwent colposcopy, 114 underwent LEEP, and 27 underwent hysterectomy. There were 68 (1%) cervical cancers detected, an incidence of 500/100,000/year. Rates of lost to follow-up were 27.9% after positive VIA screen, 49.3% between colposcopic biopsy and LEEP, and 59.6% between colposcopic biopsy and hysterectomy/chemotherapy.

Conclusion: The established infrastructure of an HIV treatment program was successfully utilized to build capacity for cervix cancer screening in a low resource setting. The program manages a population with a high burden of cervical dysplasia/cancer. Using task-shifting and validated, but low-cost approaches, population-based cervical cancer screening in a rural clinical network is feasible and effective in severely resource-constrained settings. Lost to follow up is an important obstacle to cervical screening in these settings.
Poster Session II

HPV L1 PROTEIN IMMUNOCYTOCHEMISTRY AND E2/E6 RATIO IN ABNORMAL CERVICAL CYTOLOGY WITH HPV TYPE 16 SINGLE INFECTION

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Objective: The purpose was to evaluate immunocytochemistry of L1 capsid protein and E2/E6 ratio in abnormal cytology with human papillomavirus (HPV) type 16.

Methods: A total of 137 specimens were collected at Seoul St. Mary's Hospital. Cytology was evaluated by immunostaining of HPV L1 capsid protein and E2/E6 ratio of HPV 16 was performed with RT-PCR.

The immunocytochemistry were performed using Cytoactiv® HPV L1. The staining was considered positive when at least one nuclei of the cell showed red staining. The status of HPV 16 was grouped in episomal, mixed and integrated forms using E2/E6 ratio.

Results: A total of 137 cases were eligible for the study, consisting of 21 cases of ASCUS, 59 cases of LSIL, 38 cases of HSIL, and 19 cases of cervical cancer. The HPV L1 positivity were found in 52.4%, 49.2%, 42.1%, 10.5% of ASCUS, LSIL, HSIL, cancer groups, respectively. Interestingly, 89.5% of cancer cytology showed HPV L1 capsid protein negative for immunocytochemistry. The mean ratio of abnormal cytology showed significant difference according to cytology grades (ANOVA, p < 0.05). The mean of E2/E6 ratio in cancer cytology was 0.22 and significantly lower than those of the other groups (p < 0.05). Cervical cancer cytology had a prevalence of mixed form (57.9%), integrated form (36.8%) and 5.3% of episomal form.

Conclusions: The pattern of HPV L1 capsid immunocytochemistry and E2/E6 ratio showed statistical significance according to the grades of abnormal cytology. Cancer cytology expressed extremely low ratio of E2/E6.
Poster Session II

EFFECTS OF KOREA GINSENG ON THE CLEARANCE OF HPV AFTER CERVICAL CONIZATION OF CERVICAL PRECANCEROUS LESIONS

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Background and aims: Korea Panax Red Ginseng (KPRG, KRG has been known to improve the various immunological functions. HPV infection was related with development of Cervical precancerous lesions and cancer. After the local treatment of cervical HPV-related lesions, recurrence was relatively common. The present study evaluated whether treatment with KRG can prevent the HPV infection or persistence in subjects with treatment of CIN/CIS.

Methods: Thirty six subjects, treated with CIN/CIS were randomly assigned to active KRG or placebo treatment group by double blind manner. HPV typing and Pap smear and blood test including immunologic parameters were measured at baseline, 3 and 6 months visits.

Results: Fourteen subjects in KRG group (Initially 19, 5 loss to follow-up) and Nineteen subjects in placebo group (Initially 21, 2 loss to follow-up) had completed follow-up of 6 months. HPV persistence or re-infection were significantly decreased in KRG treated group compared with placebo group (1 person, 7.1% vs, 11 person, 57.9%, P< 0.05). Among immunologic parameters, % of CD19 at 6 month was increased compared with 3 month (14.3 ±4.1% at 6 month vs 11.9 ± 2.5% at 3 month ; p< 0.05).

Conclusion: KPG had prevented the re-infection or persistence of HPV in women with surgically treated HPV-related cervical lesions).
Poster Session II

FACTORS WHICH IS RELEVANT TO THE CLEARANCE OF HIGH RISK HUMAN PAPILLOMA VIRUS INFECTION OF CERVICAL INTRAEPITHELIAL NEOPLASIA 1

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Objective: To identified factors affecting the clearance of high-risk human papilloma virus (HPV) infection in women with cervical intraepithelial neoplasia (CIN) 1.

Methods: A retrospective analysis was performed on 134 high-risk HPV infected women with CIN 1 confirmed by colposcopy-directed biopsy. Patients' follow-up continued for a maximum period of 24 months. HPV DNA test was performed at every visit.

Results: 95/134 (71%) patients were free from HPV infection and 39/134 (29%) patients showed persistent infection. Age, p16 immunohistochemical staining results, high-risk HPV load at diagnosis were not different between HPV clearance group and persistence group. Mean parity in HPV clearance group was significantly higher than persistence group (p<0.001). In over 50 year old age group and multiparous women (more than 2), adjusted odd ratios for regression of high-risk HPV was 0.11 (0.015-0.821, 95%CI) 46.402 (4.792-449.299, 95%CI) respectively.

Discussion: The possibility of high-risk HPV regression increased with parity and decreased with age. Age and parity may be useful marker for the likelihood of high risk HPV infection regression. But, initial high-risk HPV load and p16 immunochemical staining results were not unrelated with high-risk HPV regression.
Poster Session II

THE INCIDENCE AND RISK FACTORS OF LOWER-EXTREMITY LYMPHEDEMA FOLLOWING RADICAL SURGERY IN FIGO STAGE I-IIA CERVICAL CANCER

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Objective: This study aimed to determine the incidence and risk factors of lower-extremity lymphedema (LEL) in women who had radical surgery with or without adjuvant radiotherapy for FIGO stage I-IIa cervical cancer.

Methods: The medical records were reviewed retrospectively on patients with histologically confirmed FIGO stage I-IIa cervical cancer. LEL related medical problems such as peripheral vascular disease, congestive heart failure or chronic renal disease were excluded. A logistic regression analysis was used to examine the relationship between variable clinical characteristics and development of LEL.

Results: We evaluated 707 patients. Of 707 patients evaluated, we excluded 92 patients who had received radiotherapy as the initial therapy and 19 patients with LEL related to medical problems. Seventy-five patients (12.6%) developed LEL. The incidence was high in patients with adjuvant radiotherapy (odds ratio: 3.47; 95% CI: 2.086-5.788; P=0.000), with 78.7% of the LEL patients having developed the condition within 3 years after initial treatment.

Conclusions: Adjuvant radiotherapy was significantly associated with development of LEL in women who had undergone radical surgery with lymphadenectomy for FIGO stage I-IIa cervical cancer. The possibility for the occurrence of LEL must be fully explained prior to treatment and patients should be provided with the appropriate preventive education. Further prospective studies are needed to confirm the incidence and risk factors for LEL.
Poster Session II

3-D ANALYSIS OF HOT SPOTS (D_{2cc}) ON ORGANS AT RISK IN IMAGE-GUIDED BRACYTHERAPY FOR CERVICAL CANCER

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Purpose: To analyze D2cc hot spot in organs at risk (OAR) for image-guided brachytherapy.

Materials and methods: Thirty one consecutive patients underwent pelvic CT scan with an empty bladder after insertion of a Fletcher applicator for high-dose-rate brachytherapy (8Gy×3). Using the linear quadratic model, the equivalent dose in 2Gy fractions (EQD2) for each OAR was calculated. For this study, hot spot exceeding dose limits were defined as ≤90Gy_{EQD2} for bladder, ≤75Gy_{EQD2} for rectum and sigmoid and ≤65Gy_{EQD2} for bowel (α/β=3Gy). D2cc hot spots were generated in 3D if total EQD2 exceeded the above dose limits. The center of the D_{2cc} volume relative to applicator position was reported as x (right→left), y (anterior→posterior), z (inferior→superior).

Results: Sigmoid and bowel had more hot spots (45%, 39%) than bladder (30%) and rectum (23%). Rectum and bladder usually had single hot spot, while sigmoid and bowel had multiple hot spots. The common locations of hot spots for sigmoid, bowel, and bladder were at the level of the endocervix which is the narrowest portion of the uterus. The mean position of rectum hot spots was located 1.9 cm inferiorly and 1.6 cm posteriorly (z, y-axis), near the posterior surface of colpostats.

Conclusion: Hot spots for the bladder, sigmoid and bowel are depend on the shape, size of the uterus and the position of applicator. The rectal hot spot is directly depend on the rectal packing.
Poster Session II

THE EFFECT OF HIGH-INTENSITY FOCUSED ULTRASOUND IN COMBINATION WITH CISPLATIN USING A XENOGRAFT CERVICAL CANCER MODEL

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Purpose: To investigate whether concurrent chemotherapy and HIFU ablation have a therapeutic role for cervical carcinoma in an athymic nude mouse model.

Design: The cervical cancer cell line SiHa was cultured and injected subcutaneously into female BALB/c nude mice. Mice (n = 8 per group) were monitored daily for tumor development and post-treatment complications. Animals that developed tumors were randomized to four groups: HIFU ablation and cisplatin (IP injection, 100 mg/mouse twice per week) treatment, cisplatin treatment alone, HIFU ablation alone, or control. The dimensions of the tumor were measured transcutaneously using a vernier caliper. Triphenyl tetrazolium chloride (TTC) staining was done to investigate the area of coagulation necrosis in the tumors.

Results: Of the 32 animals that developed tumors, 25 had tumors able to be measured through subcutaneous palpation in the pretreatment period (control, n = 7; HIFU ablation, n = 7; cisplatin, n = 6; combination of HIFU ablation and cisplatin, n = 5). In the group receiving HIFU ablation with cisplatin, tumor volume decreased significantly as compared with those of the other groups, including control and HIFU ablation or cisplatin alone. TTC staining showed that necrosis was induced in the central zone of the tumors where ablated by HIFU, and chemotherapy enhanced the effect of HIFU ablation in the combination therapy group.

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Conclusion: HIFU ablation combined with cisplatin facilitates decreases in tumor volume and increases in tumor necrosis and could be useful as another option in treating cervical cancer patients.
Poster Session II

MOLECULAR PROGNOSTIC FACTORS IN PATIENTS WITH CERVICAL CANCER TREATED WITH RADIOCHEMOTHERAPY

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Radiochemotherapy and brachytherapy is a standard treatment for patients with cervical carcinoma staged from FIGO IB2. Approximately 50% of patients present pelvic recurrence, distant metastases. The aim of the presented study was to investigate the predictive and prognostic significance of selected molecular parameters: P53, P16, BCL2, EGFR, Bax, Cox-2, CD34, MI, Ki67, SPF, S+G2M phase, tumor ploidy and percentage of aneuploid cells in patients with cervical cancer treated with radiochemotherapy and brachytherapy. Clinical parameters: FIGO stage and overall treatment time, minimum haemoglobin level before and during treatment and SCC antigen level were also analyzed.

The data of 131 patients with squamous cell carcinoma, FIGO stages IB2-IIIB and treated with radiochemotherapy and brachytherapy were studied. Univariate analysis (log-rank test and Cox model) confirmed prognostic significance of expression of BP P53 domain (p= 0.0311), MI > 40 (p= 0.0384), index Ki-67>= 52 (p= 0.0062), SPF >11 (p= 0.0269), S+G2M fraction >= 20 (p= 0.0089) and % of aneuploid cells >46 (p= 0.0167), overall treatment time (p= 0.0369), elevated after treatment level of SCC antigen (p= 0.0001) and hemoglobin level (before treatment p= 0.0057 and during treatment p= 0.0203) with regard to overall survival. For disease-free survival univariate analysis confirmed important prognostic significance of: MI>40 (p= 0.0367), Ki-67 >= 52 (p= 0.0044), SPF>6 (p= 0.0059), S+G2M fraction >20 (p= 0.0329), percentage of aneuploid cells >47 (p= 0.0404), overall treatment time (p= 0.0121), hemoglobin level (p= 0.0075 for Hb before treatment and p= 0.0112 for Hb during treatment) and FIGO stage (p= 0.0222).
Poster Session II

EVALUATING RELAPSE PATTERNS OF CERVIX CANCER PATIENTS TREATED WITH DEFINITIVE RADIOTHERAPY

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Objectives: To evaluate recurrence patterns among cervix cancer patients treated with definitive radiotherapy.

Methods: Patients with FIGO stage IB-IVA cervix cancer treated from 1991 to 2007 with pelvic radiotherapy (+/- chemotherapy) followed by brachytherapy developing recurrences were analyzed.

Results: Of 222 cervix cancer patients, 99 (45%) developed recurrences, and since 2000 when chemotherapy use became routine, there have been fewer relapses, 35% vs. 49% (p=0.05). The median time to relapse was 11 months and 91% of relapses occurred within 3 years. Eighty-one percent of relapses were symptomatic and 12% were diagnosed on imaging. The sites of recurrence were as follows: 16% pelvis, 8% para-aortic nodes, 4% lung, 11% multiple sites and 5% other. There were 16% in-field recurrences, 21% out-of-field, and 7% with a combination. Only 3% (1/36) of patients with in-field relapses underwent salvage curative therapy (pelvic exenteration) compared with 35% (6/17) of patients with out-of-field recurrences isolated to the para-aortic nodes (treated with radiation +/- chemotherapy/surgery). For these salvage treatment patients, long-term survivors (>5 years) were only amongst those with para-aortic failure - 50% (3/6). Median survival after diagnosis of recurrence for all relapsed patients was 7.5 months, but 28 months for patients treated aggressively for salvage.

Conclusion: The most common sites of relapse were within the pelvic and para-aortic regions, and almost all occurred within 3 years. Recurrences were usually symptomatic, and salvage therapy was not commonly used. Although successful salvage of recurrences was infrequent, outcomes were best for those with isolated para-aortic relapses treated with radiation.
Poster Session II

INCIDENCE RATE AND LOCALIZATION OF LYMPH NODE METASTASES IN PATIENTS WITH INVASIVE CERVICAL CANCER

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Objective: To establish the incidence rate, localization and distribution of lymph node metastases FIGO stages I and II.

Material and methods: Between 2002 - 2011 294 patients FIGO stages ( IB1 - IIB ) had been operated on ( IB1 - 110; IB2 - 98; IIB - 86 ). The surgical management consisted in radical hysterectomy class III and pelvic lymphadenectomy. In cases with enlarged paraaortic lymph nodes - paraaortic lymphadenectomy was performed.

Results: Lymph nodes metastases ( LNM ) were detected in 82 patients (27,8%). The number of LNM were 1 to 3 in 66 patients (22,4%) and more than 3 - in 16 women (5,4%). Pelvic LNM were found in 74 patients (25,17%) and paraaortic LNM - in 8 patients (0,34%). LNM were evaluated as macrometastases in 45 women (15,31%) and as micrometastases - in 37 women (12,59%). The incidence rate of LNM in stage IB1, IB2 and IIB was 20,9%, 33,67% and 30,24%, respectively.

Conclusion: Bulky cervical lesions even tough in stage IB1 reveal higher aggressiveness and metastatic potential than small cervical lesions.
Poster Session II

TREATMENT OF CERVICAL CARCINOMA IB2 STAGE
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Objective: To establish the overall and disease-free survival (OS and DFS) in patients IB2 stage FIGO with primary surgical treatment or operated on after preoperative RT.

Material and methods: Between 2003-2011 98 patients (FIGO IB2 stage) were operated on. 83 patients were submitted to primary surgery (radical hysterectomy class III with pelvic lymph node dissection - group 1 and 11 were operated on after preoperative RT - 30 Gy - group 2. All operated patients were submitted to adjuvant RT - 52 Gy. Four patients were operated on after NCT (neoadjuvant chemotherapy). All patients were followed between 2 and 96 months - median period of 45 months.

Results: The actuarial OS and DFS for all patients were estimated as 73.5% and 75.6% respectively. The OS and DFS for group 1 were estimated as 73,5% and 74,7% respectively.

The OS and DFS for group 2 were estimated as 72,8% and 82% , respectively.

Conclusion: Stage IB2 cervical cancer is related to worse prognosis in comparison to IB1 FIGO stage, because of the higher incidence of distant metastases. Preoperative RT doesn't change the oncological outcomes. There is no statistical difference between group 1 and group 2 in terms of survival. Is important to perform paraaortic lymph node dissection and concurrent radiochemotherapy in these patients.
Poster Session II

PROGNOSTIC FACTORS SIGNIFICANCE AND IMAGE-GUIDED RADIOTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER (LACC) PATIENTS UNDERGONE RADICAL SURGERY

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342 patients with verified LACC were included. 246 pts. in AB-group of modified postoperative radiotherapy - MPORT (A - 152 pts. after primary surgery, B - 94 pts. after surgery with previous taxan-platinum based chemotherapy), 96 pts. - in retrospective C-group after conventional postoperative radiotherapy. 20 clinico-morphological parameters were picked out, analyzed with Cox multivariate regressive analyses and compared as significant factors for tumor progression. Primary tumor volume over 30 cm³ (HR 1.64, 95% CI 1.07-2.51, P=0.024); cervical stroma invasion over 1/3 (HR 1.60, 95% CI 1.11-2.31, P=0.011); uterine involvement with myometrium invasion >5 mm (HR 1.38, 95% CI 1.04-1.84, P=0.026); parametrium or vagina involvement (HR 1.86, 95% CI 1.23-2.82, P=0.003); pathomorphosis 0-I Grade after neoadjuvant radiotherapy (HR 1.54, 95% CI 1.03-2.31, P=0.036); positive resection margin (HR 1.81, 95% CI 1.35-2.41, P=0.002); tumor embolus in lymphatic and blood vessels (HR 1.79, 95% CI 1.19-2.68, P=0.005); lymph node metastases (HR 1.86, 95% CI 1.13-3.04, P=0.014); cytoreductive surgery (HR 2.01, 95% CI 1.28-3.16, P=0.002); heavy intraoperative bleeding with persistant anemia II-III (HR 1.49, 95% CI 1.15-1.95, P=0.003) significantly decrease DFS in control group, which became a basis for PORT image-guided modification with dose and volume individual choice. OS and DFS significant improvement was shown in AB-group (60-month OS 74.0±2.9% vs 41.6±5.3%, DFS 71.9±4.6% vs 57.9±4.0% (P< 0.001), with 15% increase after neoadjuvant chemotherapy. For Cox analyses, uterine-vagina involvement, positive margin, LVI and obturator LN metastases negative influence was overcome during MPORT. Parametrium involvement, residual tumor after surgery, ineffective neoadjuvant therapy still significantly decreased DFS.
Poster Session II

STUDY OF OUTCOME AFTER CONCURRENT CHEMORADIOTHERAPY FOR ADVANCED CERVICAL CANCER WITH INVASION TO UTERINE CORPUS

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Objective: It's been a long time since standard treatment for advanced cervical cancer is concurrent chemoradiotherapy. Its prognosis is affected by metastases or recurrence after treatment. We studied whether invasion to the uterine corpus in advanced cervical cancer gives influence to the prognosis.

Methods: A total of 206 cervical cancer (squamous cell carcinoma) stage Ib1-IVa patients who underwent chemoradiotherapy between 2000 and 2010 were enrolled and retrospectively analyzed. Determination of the invasion to uterine corpus was carried out by MRI. In this study, if the cervical tumor has invaded beyond the internal os of the cervix, we have determined it as "invasion to corpus".

Results: The recurrence rate was 27.2% (56/206). In this study, "tumor size", "invasion to corpus", and "para-aortic lymph node swelling" were independent risk factors of distant recurrence on multivariate analysis. The 5 year disease free survival rate of "invasion to corpus" group (62.5%) was significantly worse than that of "non invasion to corpus" group (79.0%) (p=0.0172 Log-rank test).

Conclusion: Our result suggests that "invasion to corpus" in cases of the patients with advanced cervical cancer who underwent concurrent chemoradiation therapy might be a risk factor for distant recurrence.
Poster Session II

ARE DNA REPLICATION LICENSING FACTORS (RLFS) LINKED TO TUMOUR CELL CYCLE STATE AND CLINICAL OUTCOME IN CERVICAL CANCER?

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Introduction: DNA replication licensing factors play a crucial role in the control of proliferation, differentiation and maintenance of genomic stability. Multiparameter analysis has shown a relationship between these regulatory proteins expression, tumour cell cycle state, and clinical outcome in penile, ovarian and breast cancers.(Refs available)

Objective: A Pilot study using a panel of cell-cycle biomarkers to assess whether a significant difference in proliferation signatures exists in cervical cancer reflecting a difference in cell-cycle phenotypes.

Design: In a cohort of 35 patients with cervical cancer (stage IB2-IVA) all treated with neoadjuvant chemotherapy followed by chemoradiation, we attempted to link protein expression profiles of the standard proliferation marker Ki67 and the RLFS Mcm2 and Geminin to clinicopathological variables (stage, grade) and clinical outcome.

Results and conclusions: Although the numbers are small (n=35), there appears to be no significant relationship between the levels of biomarker expression and tumour differentiation (p=0.39), tumour stage or clinical outcome , suggesting that only one aggressive cell cycle phenotype exists in cervical cancer; all cancers showed an accelerated cell cycle progression (actively cycling). This is not the case in Breast cancer as shown by Loddo et al 2009, with cell-cycle-phase progression analysis identifying three different phenotypes with prognostic and predictive significance. A larger study is needed to investigate cell-cycle progression analysis and any predictive or prognostic significance in Cervical Cancer, given the aggressive nature of this disease.
Poster Session II

PREVALENCE AND DISTRIBUTION OF HIGH RISK HUMAN PAPILLOMAVIRUS (HPV) IN KARNATAKA, INDIA

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Background: In view of conducting HPV vaccination in India it is most important to understand the prevalence of HPV genotypes in this population, not only in squamous cell carcinoma of cervix and oral cavity but also in the general population. In this study we explored the prevalence and distribution of high-risk HPV types 16 and 18 in carcinoma of cervix, saliva of patients with oral squamous cell carcinoma and in general population in Karnataka.

Methods: Cervical cancer specimens after punch biopsy (n=60) were obtained from women attending associated hospitals. Saliva rinse of (n=34) OSCC patients and (n=396) normal individuals from different regions of North Karnataka, were collected and PCR based high-risk HPV genotyping was carried out.

Results: Using consensus PCR primers it was observed that 96.7% patients were infected with HPV irrespective of specific type in cervical cancer. Among them, HPV 16 was observed in 89.7%, HPV 18 in 86.2% and both HPV 16 and 18 in 79.3% patients. In OSCC, 70.6% were positive for HPV, among which HPV 16 prevalence was observed in 45.8%, HPV 18 in 54.2%, and HPV 16 and 18 multiple infection in 4.18%. In general population, HPV prevalence was observed in 84.4%. Among them, HPV 16 was observed in 2.75% and HPV 18 in 22.0% patients. In general population, multiple infection with HPV 16 and 18 was not observed but 75.3% were found to be infected by HPV genotypes other than HPV 16 & 18.

Conclusions: Our study reveals that multiple infection of HPV 16 and 18 is quite high in cervical cancer and in case of OSCC. In general population HPV 18 prevalence was observed to be high. With this, we can conclude that both HPV 16 and 18 vaccinations will reduce the burden of cervical cancer and OSCC in Karnataka.
Poster Session II

CASPASES AS PUTATIVE PREDICTIVE BIOMARKERS OF CERVICAL CANCER DEVELOPMENT AND PROGRESSION

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Background: Molecular mechanisms underlying HPV-induced immune failure and contributing cervical cancer development are in focus of investigation. Induction of apoptosis of immune cells and its contribution to overall immune dysfunction are still arguable in respect to cervical malignancy. We questioned if caspases, the key members of apoptotic signaling pathways, could be indicative of immune suppression and, on the other hand, if they could be helpful in revealing the formation of tumor cells’ resistance to apoptosis.

Aim: To investigate the expression of caspases -3,-6,-8,-9 in peripheral blood leukocytes (PBLs) and tumor tissue of patients with intraepithelial neoplasias, carcinoma in situ or cervical cancer stage I-IV.

Methods: Caspase expression at mRNA level and proteolytic activity were evaluated by real-time PCR and spectrofluorometry, respectively. The number of CD95-positive PBLs was monitored by fluorescence microscopy.

Results: The increase of surface CD95 expression, caspases -3,-6,-8 mRNA content and activity was shown in PBLs with disease progression. In intraepithelial neoplasia tissue samples, both increase and decrease of caspase mRNA and protease activity were observed. In stage I-IV tumors we detected discrepancy between the two levels of regulation - significant decrease in enzymatic activity but increase in mRNA relative content.

Conclusions: Our results point at activation of Fas-dependent apoptosis in PBLs of cervical cancer patients and support the emerging data that inhibition of caspase activity as a mechanism of tumor cell survival is relevant to cervical cancer. The work was supported by the Government of the Russian Federation (contract numbers 11.G34.31.0052 and 14.740.11.1034).
Poster Session II

FACTORS OF PROGNOSIS AND OF RESULTS OF CERVICAL CANCER TREATMENT

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This investigation includes 510 patients with I-II stage (FIGO 1997) of cervical cancer undergoing surgery, radiation or combined modality treatment. The main group includes 259 of elderly and senile, compared group a younger (18 to 45 years) patients.

It was found that adequate methods of cervical cancer treatment of elderly and senile patients of Ia stage of disease are pan hysterectomy with upper third of vagina, and of Ib-Ila stage - different combination of surgical interference (such as Wertheim operation) combined with radiotherapy.

Common 5-years survival of elderly, senile and younger patients with cervical cancer has reliable distinctions only under combined therapy (76.4% and 93.5% respectively, p=0.05).

Factors of unfavorable prognosis for elderly and senile patients with cervical cancer compared with the young patients are as following: depth of tumor invasion in cervix stroma more than 1 sm; involvement of all vaginal part of cervix; endocervical form of anatomic growth of tumor and metastatic involvement of regional lymph nodes.
Poster Session II

SEXUAL FUNCTIONING OF CERVICAL CANCER SURVIVORS: A REVIEW WITH A FEMALE PERSPECTIVE

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Objective: Sex is an important, often deteriorated, dimension of quality of life after cancer treatment. We conducted a systematic review on sexual functioning of cervical cancer survivors.

Methods: Studies between January 1988 and April 2010 were rated on their internal validity. Results were analyzed focusing on four major categories of sexual functioning: desire, arousal, orgasm, pain. Comparisons were made between healthy controls versus cervical cancer survivors, survivors before versus after treatment and between different treatment modalities.

Results: Twenty studies were included. Most studies showed no differences in the ability to achieve an orgasm. Cervical cancer survivors reported more dyspareunia than healthy controls and dyspareunia was more frequent and lasted longer after radiotherapy. Lack of lubrication was more frequent in cervical cancer survivors and a significant decrease in sexual interest and activity after treatment was found.

Conclusion: Cervical cancer survivors are at risk for sexual pain disorders, while sexual satisfaction (orgasm) is not impaired and radiotherapy negatively influenced sexual pain disorders. Health care providers should inform cervical cancer survivors about the possible risk of developing sexual pain disorders after cervical cancer treatment, especially after radiotherapy. As sexual satisfaction per se is not impaired, we suggest that prevention and treatment of sexual dysfunction should focus on painless and satisfactory sex instead of on resuming intercourse.
Objective: Lymph node involvement is one of the most important prognosis factors. The sentinel lymph node procedure is a recent technique. Aberrant lymph node spread can lead to misdiagnose the lymph node involvement and undertreat patients. The goal of this study is to evaluate the first ten cases of sentinel lymph node biopsy detected by a combination of with a SPEC-CT and intraoperative detection by laparoscopy of the sentinel lymph node with blue patent dye and technetium.

Material and method: First 10 patients with a cancer of the cervix stage IA2 and IB1 had a SPECT CT prior to the sentinel lymph node biopsy by laparoscopy. The surgery was performed the day after the injection of a combination with nanocis and technetium. When the laparoscopy was placed an injection of patent blue dye was performed. The sentinel node was then identify regarding the SPECT CT prior the surgery, the patent blue dye and the use of a gammaprobe during the surgery.

Results: Eight patients had bilateral pelvic sentinel nodes. Two patients had common iliac artery sentinel nodes. Only one patient had a micrometastasis wich was detected in final pathology. This lymph node was at the level of the iliac bifurcation artery.

Conclusions: The SPECT CT helps the surgeon in order to anticipate the anatomical site of the sentinel node before the laparoscopy. Two aspects are relevant: the detection of aberrant pathway of spread and the better detection of micrometastasis by the pathology technique of analysis of the sentinel node.
Poster Session II

MANAGEMENT OF ADENOCARCINOMA IN SITU OF THE UTERINE CERVIX: A COMPARISON OF LOOP ELECTROSURGICAL EXCESION PROCEDURE & COLD KNIFE CONE

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Objective: The aim of this study was to compare loop electrosurgical excision procedure (LEEP) to cold knife conization (CKC) as therapeutic management procedures for women with ACIS of the cervix.

Methods: A retrospective chart review of all patients who underwent a conization procedure with a preoperative or postoperative diagnosis of ACIS of the cervix from 1997 to 2011. Data gathered included demographics, risk factors, pretreatment Pap and colposcopic biopsy results, conization pathology including presence of invasive cancer and margins status, subsequent need for re-conization or hysterectomy, and follow up. Outcome measures, such as diagnosis of invasive cancer, negative margins, and recurrence of ACIS or development of invasive cancer, were compared between LEEP and CKC.

Results: Of 115 conization procedures performed, 61 were LEEP (31 diagnostic and 30 therapeutic) and 54 were CKC (6 diagnostic and 48 therapeutic). CKC patients were more often nulliparous, on oral contraceptive pills, and smoking cigarettes than LEEP patients. For the 78 patients who underwent conization procedures with therapeutic intent, there were no differences in rates of positive margins (20% vs 17%), invasive cancer (3.3% vs 4.2%), recurrence of ACIS (10% vs 8.3%), or subsequent development of invasive adenocarcinoma (0 vs 2%) between LEEP and CKC, respectively.

Conclusions: In our study, LEEP was as good as CKC for treatment of ACIS of the cervix, achieving the same rates of negative margins, diagnosis of invasive cancer, and recurrence of ACIS or invasive cancer.
Poster Session II

EFFECTIVENESS OF A SURGICAL RADIOPROTECTION AT THE TIME OF THE STAGING OF LOCALLY ADVANCED CERVIX CANCER

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Definitive chemoradiation therapy is the commonly admitted management of locally advanced cervix cancer (LACC). However it results in significant 10-15% early and 5-7% grade 3-4 distant toxicity. The aim of this study was to test the effectiveness of radioprotective measures at the time of the surgical staging.

Material and methods: The procedure consists, after the paraaortic dissection, to prepare an omental mesh, detached from the right 2/3 of the transverse colon. It is fixed in the Douglas pouch to move the rectum away from the cervix. Then, the sigmoid loop is retracted high in the paracolic gutter and fixed by clips.

Results: From 2010 to 2012, 23 stage IB2-IVA LACC patients were submitted to this protocol, after informed consent. No intra nor postoperative complication was observed so far. According to patients's natural adiposity (mean BMI was 25.6 kg/m² (18.3-47.3)), the volume of retrouterine omental mesh averaged 18 cc (5-25) (MRI-based assessment). This interposition translated into a risk of quite zero of radio-induced rectal complication when delivering the brachytherapy dose. In addition, this protection was constant throughout treatment duration.

Conclusion: Although unfrequent, radio-induced rectosigmoid complications can be a durable and life-threatening problem. These simple procedures may reduce their incidence while not altering the quality of treatment.
Poster Session II

CLINICAL SIGNIFICANCE OF THE MAXIMAL STANDARDIZED UPTAKE VALUE FOR F-18 FLUORODEOXYGLUCOSE IN CERVICAL CANCER AS AN INDICATOR OF PROGNOSIS

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Objectives: We evaluated the prognostic significance of tumor metabolic activity on pretreatment positron emission tomography using the glucose analog F-18 fluorodeoxyglucose (FDG-PET) in patients with FIGO stage II-IV cervical cancer.

Methods: We reviewed the medical records of 65 consecutive patients with stage II through IV cervical cancer who underwent pretreatment FDG-PET studies at Korea Cancer Center Hospital between Feb. 2001 and May. 2007. Pretreatment FDG uptake of the primary tumor was assessed with the semiquantitative standardized uptake value (SUV) and correlated with progression-free and overall survival. Maximal Standardized Uptake Value (SUVmax) and sites of lymph node metastasis were reviewed. Survival was estimated by the Kaplan-Meier method.

Results: The median follow-up of all patients was 30.5 months (range 1.3 to 87.1 months). The mean SUVmax within the primary cervical cancer in all patients was 10.8 (range, 3.2-28.7). Most of patients had squamous histology (56 patients; 86.2%). 83.1% of patients were treated with concurrent chemoradiation. Three-year progression-free survivals in patients with maximal SUV < 10.0 and >10.0 were 52.8% and 25.0% (P = 0.028) respectively, while overall survivals were 55.2% and 51.6% (P = 0.7), respectively.

Conclusion: FDG uptake within primary cervical cancer, as measured by SUV, is predictive of progression-free survival in patients with FIGO stage II-IV cervical cancer.
Poster Session II

FALSE POSITIVE PELVIC LYMPH NODE ASSOCIATED FACTORS IN CERVICAL CANCER

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Objective: Aim of this study is to evaluate the factors affecting on the preoperative false positive pelvic lymph on clinical and baseline study for early cervical cancer.

Methods: We retrospectively analyzed the medical records of 74 patients who were diagnosed with cervical cancer with stage 1A or 1B1 at Ulsan University Hospital between March 2007 and November 2011. The methods of preoperative image included AP-CT, Pelvic MRI, and PET-CT.

Results: Median patient age was 48.0 (range, 30-73) years. The total 22 patients showed the positive pelvic lymph on a preoperative imaging work-up. The eleven patients out of the imaging positive 22 patients were truly pathologically positive (50%, 11/22). The others were false positive group. There were no significant difference in age (p=0.324).

The interval from the date of performing the biopsy to the date of undertaking image had no significant difference (p=0.458) and the interval from the date of performing the biopsy to the date of the operation (p=0.292) between the two groups.

The five patients of the 22 patients with pathological positive results had false positive results on PET-CT.

The four patients of the eleven patients with the positive result in both MRI or AP-CT and pathological finding were positive on PET-CT (true positive rate =36.4%). The true negative rate was 63.6%.

Conclusion: To reduce a false positive lymph and undertake radical operation, our study suggested that it is necessary to find factors affecting on false positive results on preoperative image studies and to correct these factors.
Poster Session II

METHYLATION STATUS OF CERVICAL CARCINOGENESIS: EVALUATION OF CERVICAL CYTOLOGY WITH HUMAN PAPILLOMAVIRUS TYPE 16
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Objective: It has been reported that DNA hypermethylation occurs during the process of cervical carcinogenesis. The aim of this study is to evaluate the status of hypermethylated genes of cervical cytology according to the degree of cervical disease in Korean women.

Methods: We used methylation-specific polymerase chain reaction to analyze hypermethylation of 4 genes (PAX1, CADM1, ADCYAP1 and MAL) in 122 cervical specimens, including 29 cervical intraepithelial neoplasia (CIN) grade I, 4 CIN II, 42 CIN III, 18 cervical cancer, and 29 normal cervix.

Result: We observed that 4 genes (PAX1, CADM1, ADCYAP1, MAL) were more frequently methylated in cervical cancer (83.3, 77.8, 88.9, and 72.2 %, respectively) than in normal (0, 3.4, 3.4, and 6.9%). ROC curve demonstrated that methylation of the 4 genes discriminated between high grade cervical lesions (≥CIN 3) and low grade cervical lesions (< CIN3). The estimated specificities of these 4 genes for detecting high grade lesion were 100, 96.6, 96.6 and 93.1% (p = 0.0001). And the estimated sensitivities of that were 83.3, 77.8, 88.9 and 93.1% (p = 0.0001). Additional ADCYAP1/PAX1 methylation analysis on the HPV16-positive women increased the sensitivity to 88% with specificity to 96.7% (P < 0.001).

Conclusion: Methylation of the PAX1, CADM1, ADCYAP1 and MAL is significantly associated with the development of ≥ CIN3, which could be used for molecular marker for cervical carcinogenesis in Korean women.
Poster Session II

PLATINUM-BASED COMBINATION VERSUS WEEKLY CISPLATIN DURING ADJUVANT CONCURRENT CHEMORADIATION AFTER RADICAL HYSTERECTOMY IN EARLY CERVICAL CANCER WITH PELVIC LN METASTASIS


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Objective: Adjuvant concurrent chemoradiation (CCRT) should be considered in surgically treated patients with early stage cervical cancer (ECC) who exhibit pelvic lymph node (LN) metastasis; platinum-based chemotherapy is usually recommended during adjuvant CCRT. However, it is unclear which regimen has better prognostic outcomes.

Methods: We reviewed electronic medical records to find patients with primary ECC (FIGO stages IB-IIA) who underwent type III radical hysterectomy and adjuvant CCRT due to pelvic LN metastasis at Samsung Medical Center, Sungkyunkwan University School of Medicine in Seoul, Korea, between November 1997 and September 2007.

Results: Among the 75 patients, 34 received weekly cisplatin. Combination chemotherapy was performed without consolidation in 21 patients and with consolidation in 20 patients. The mean follow-up period was 59.0 months and the five-year survival rate was 84.4%. In multivariate analysis, combination chemotherapy ± consolidation was associated with improved disease free survival (HR, 0.23; CI, 0.06-0.88; p=0.032, and HR, 0.29; CI, 0.09-0.91; p=0.034); combination chemotherapy with consolidation significantly improved overall survival (HR, 0.11; CI, 0.02-0.87; p=0.037) when compared to weekly cisplatin.

Conclusion: We observed platinum based combination chemotherapy during adjuvant CCRT after surgery promoted better survival than a weekly cisplatin regimen in ECC patients with pelvic LN metastasis. Consolidation chemotherapy after adjuvant CCRT may contribute to the increased survival in these patients.
Poster Session II

THE EXPRESSION OF SYNAPTONEMAL COMPLEX PROTEIN 3 (SCP3) AND PHOSPHO-AKT IN CERVICAL NEOPLASIAS


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Purpose: Synaptonemal complex protein 3 (SCP3) is a marker for cell transformation, and it has been shown that the overexpression of SCP3 in tumor cells could lead to activation of AKT. This study explored expression of SCP3 and its relationship with the phosphorylated AKT (p-AKT) in cervical neoplasias.

Materials and methods: Five hundred eighty eight cervical tumor samples and matched normal epithelial samples were arrayed into tissue microarrays. The status of SCP3 and p-AKT was studied using immunohistochemical analysis. Staining results for each antibody were compared with clinical and pathologic features, and the relationship between staining results was explored.

Results: Expressions of SCP3 and p-AKT were significantly increased in cervical cancer cases compared with normal epithelia (P < 0.001, each). Increased SCP3 expression was observed in patients with increasing tumor stage (P = 0.002) and tumor grade (P < 0.001). In multivariate analysis, disease-free survival in cervical cancer patients was significantly shorter in cases with overexpression of SCP3 (HR = 4.81 [1.37-16.95], P = 0.014), lymph node metastases (HR = 3.07 [1.23-7.67], P = 0.016), and advanced tumor stage (HR = 2.74 [1.09-6.88], P = 0.032). SCP3+/p-AKT+ expression (P =0.034) and increased tumor stage (P = 0.006) showed shorter overall survival by Kaplan-Meier analysis.

Conclusions: This study shows that SCP3 expression in addition to p-AKT predicts poor prognosis in cervical cancer. Moreover, the correlation between expressions of SCP3 with p-AKT indicates that SCP3 activation through the AKT pathway plays an important role in the progression of cervical cancer.
Poster Session II

SEXUALLY RESPONSIBLE BEHAVIOUR AMONG ADOLESCENTS FOR PREVENTION OF CERVICAL PRECANCEROUSES

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HPV is one of the most frequent sexually transmitted diseases in the world. Vaccine to immunise against HPV infection would be a valuable strategy for the primary prevention of cervical cancer. Sexually active adolescents face serious health risks associated with unprotected sexual intercourse. In period from 2005-2011, a survey was conducted on a sample of 380 female adolescents in the Zagreb area and 190 girls in Jastrebarsko area. The purpose of the survey was to indicate the difference in HPV types among urban and rural adolescents and their impact on appearance of pathologic changes on the cervix. The following examinations and tests were carried out: gynaecological exam, Pap test, colposcopy, including taking of epidemiologic anamnesis. HPV genotyping was carried out by application of polymerase chain reaction method. The hypothesis was that HPV infection risk is higher in urban than in rural areas. Epidemiological anamnesis were analysed: contraception methods used, hygiene habits, smoking of cigarettes, number of sexual partners and the period from the first intercourse to the appearance of cervical dysplasia. Absolute values of HPV appearance were analysed by statistical tests. Conclusions based upon given results: With correct and timely application of cytology, colposcopy and targeted biopsy in adolescents with cytological picture of dysplasia, accuracy of the diagnosis is increased, unnecessary conisation is avoided, and the follow up period is reduced. The most important factor in prevention of CIN is recognizing high risk adolescents. The most effective prevention of sexually transmitted diseases is a stable, harmonious relationship, with a faithful partner. Also a physical and mental maturity of both partners. For systematic prevention it is necessary: introduce an effective sexual education in schools starting from primary school, develop interdisciplinary cooperation between social and medical sciences, including all experts. We organized educational project for adolescents about sexual responsible behaviour "Knowledge is pleasure". In appropriate assembly rooms of Secondary Schools of Zagreb educational lectures held by medical specialists and after the lectures multimedia presentations were held.
Poster Session II

HPV-16 E6/E7 INDUCES CELL MIGRATION AND INVASION IN CERVICAL CANCER BY REGULATING CADHERIN SWITCHING IN VITRO AND IN VIVO  

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Persistent infection of high-risk human papillomavirus (HR-HPV) has been recognized as a necessary cause of cervical carcinogenesis. However, the roles of viral oncogenes of HR-HPV on the progression of cervical cancer are still unclear. Cadherin switching, as one of the key characteristics of epithelial-mesenchymal transition, contributes to cancer metastasis. But, the regulatory effect of HR-HPV E6/E7 on cadherin switching and its possible mechanisms remain unexplored. In current study, we positively or negatively regulated the expression of E6/E7 in Hacat, Siha or Caski cells. Cellular growth and apoptosis was tested by MTT and flow cytometry respectively, and cell migration and invasion was examined by wound-healing assay or transwell invasion assay. Additional, 8×10^6 of siRNA transfected Siha or Caski cells were subcutaneously separately injected into BALB/C mice. Tumor volume and growth curves were assessed. E-cadherin, N-cadherin and P-cadherin mRNA and protein expression were detected by qRT-PCR and immunoblotting in vitro, and by immunohistochemical staining in vivo. We found that cellular proliferation, apoptosis, migration and invasion were altered in cells in which the expression of HPV-16 E6/E7 was up- and down-regulated, and tumor volumes were decreased and survival time was prolonged in BALB/c mice inoculated cells with HPV-16 E6/E7 silencing. Again, the expression levels of E-cadherin, N-cadherin and P-cadherin mRNA and protein were changed by regulating HPV-16 E6/E7 in vitro and in vivo. Thus, our findings first suggest, to our knowledge, that HPV-16 E6/E7 induces cell invasive potential via regulating cadherin switching, and could consequently contribute to the progression of cervical cancer.
Poster Session II

ABDOMINAL RADICAL TRACHELECTOMY FOR CERVICAL MALIGNANCIES: SURGICAL, ONCOLOGICAL AND FERTILITY OUTCOMES IN 107 PATIENTS

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Objective: To report our experience of abdominal radical trachelectomy (ART) for patients with cervical malignancies.

Methods: We conducted a retrospective review of a prospectively maintained database of patients undergoing fertility-sparing ART for cervical malignancies at our institution from 04/2004 to 03/2012.

Results: 107 patients with cervical malignancies underwent laparotomy for planned ART. Three needed immediate completion of radical hysterectomy due to unfavorable intraoperative findings. Median age was 28.3 years (11-42). Histology included 11(10.58%) adenocarcinoma, 83(79.81%) squamous carcinoma, 4(3.85%) adenosquamous carcinoma and 6(5.77%) botryoid sarcoma. Median number of nodes evaluated was 25 (12-53); Eighteen (17.31%) patients with pathologic risk factors received adjuvant therapy. Twenty-six of 66 IB1 cases had tumor size > 2cm. One recurrence was observed at a median follow-up of 27.2 (1.5-95) months. Five (4.81%) developed postoperative cervical stenosis - all occurred before we started to routinely install T-IUDs during the procedure. Forty-eight patients completed the survey which aimed to understand what factors influenced reproductive outcomes. For various reasons, 12 patients attempted to conceive and 4 succeeded. Three of them delivered by cesarean section after 39 weeks and one is currently pregnant.

Conclusions: ART seems to be a reasonable option for selected patients whose tumors are no larger than 4cm when conducted by experienced gynecologic oncologists. The main postoperative complication is cervical stenosis, which could be effectively prevented by installation of a tailed T-IUD during the surgery. Social, familial and physical factors can largely influence the patients' reproductive outcomes. Issues of reproductive concerns and quality of life require further investigation.
Poster Session II

PARA-AORTIC LYMPH NODE (PAN) ASSESSMENT AND ITS SURGICAL INDICATION IN PATIENTS WITH STAGE IB-IIA CERVICAL CANCER

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Objective: To investigate the frequency of PAN involvement in stage IB-IIA cervical carcinoma and to determine the indication of para-aortic lymphadenectomy.

Methods: Medical records of 517 patients with Stages IB-IIA cervical carcinoma who underwent radical hysterectomy and systematic pelvic and PAN dissection from 2005 to 2010 were investigated retrospectively. 522 patients with matched clinical pathological factors who underwent para-aortic lymph node biopsy during the same period were selected as control group.

Results: The frequency of PAN involvement was 9.67% (50 patients) in the study group. All of the patients with positive PAN had pelvic nodal metastasis while 16 (32%) had no common iliac lymph node metastasis. FIGO Stage, tumor size, and pelvic nodal involvement were independent risk factors for PAN metastasis through multivariate analysis. The ROC curve showed optimal cut off point of tumor size to predict PAN metastasis was 3cm (sensitivity, 94.1%; specificity, 44.6%). Median follow-up was 33 (8-53) months. Two-year DFS of patients in the study group was not statistically improved when compared to that in the control group. However, for patients whose tumor was no less than 3cm, systematic PAN dissection significantly improved DFS (85.1% in the study group vs. 78.3% in the control group, p=0.031). Mean operating time for para-aortic lymphadenectomy was 30 (20-45) minutes and the rate of surgical complications was 7.7%.

Conclusion: PAN dissection is safe and feasible for cervical cancer patients. It is recommended systematic paraaortic lymphadenectomy be routinely offered for stage IB-IIA cervical cancer patients whose tumor size is no less than 3cm.
Poster Session II

FERTILITY-SPARING SURGERY FOR PEDIATRIC (adolescent) PATIENTS WITH BOTRYOID RHABDOMYOSARCOMA INVOLVING THE UTERINE CERVIX

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Background: Botryoid rhabdomyosarcoma of the uterine cervix, which is most often seen arising in the adolescents, is extremely rare. In the past, this tumor was best treated with pelvic exenteration and chemoradiation.

Objective: To report our experience on fertility-sparing treatment with this disease. To discuss proper selective criteria and type of surgery for fertility-sparing treatment with this disease.

Methods: We conducted a retrospective review of a prospectively maintained database of patients undergoing fertility-sparing surgery for cervical botryoid rhabdomyosarcoma at our institution from 08/2006 to 03/2012.

Results: We presented here seven pediatric (adolescent) patients with botryoid rhabdomyosarcoma involving the uterine cervix. All these cases were offered fertility-sparing surgery. The first patient was offered cervical conization while other six patients underwent radical abdominal trachelectomy and pelvic lymph node biopsy. They all accepted multiagent chemotherapy and presented with favorable outcomes.

Conclusion: In properly selected cases of cervical botryoid rhabdomyosarcoma, conservative surgeries should attempt to preserve reproductive function without compromising in survival. Radical abdominal trachelectomy and pelvic lymph node biopsy have appeared to secure local disease control better than other minimal invasive surgeries (eg, cervical conization). Radical abdominal trachelectomy with skills preserving uterine arteries may allow sufficient blood supply to maintain uterine viability and achieve future fertility, and thus benefit the pediatric (adolescent) patients.
Poster Session II

TREATMENT OUTCOMES AND PROGNOSTIC FACTORS IN CERVICAL CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY PLUS SURGERY

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Purpose: To evaluate the treatment outcomes and prognostic factors, and to determine the indication for adjuvant radiotherapy in cervical cancer patients treated with neoadjuvant chemotherapy (NACT) plus surgery.

Methods and material: From 2000 to 2008, 61 patients with stage IB-IIA cervical cancer received NACT plus surgery. Among them, 31 patients received adjuvant radiotherapy with (n=26) or without (n=5) chemotherapy. Pretreatment [initial tumor size (iTS), radiographic lymph node (rLN) metastasis] and postoperative [intermediate risk factor, combinations of 2 or more following factors: lymphovascular space invasion; pathologic tumor size; deep stromal invasion, high risk factor, one or more following factors: positive resection margin; pathologic LN metastasis; parametrial invasion] prognostic factors were analyzed. There were a higher proportion of patients with high or intermediate risk factor in patients treated with adjuvant RT. The median duration of follow-up was 62.9 months.

Results: The 5-year overall survival (OS) and progression free survival (PFS) rates were 88.1% and 84.4%, respectively. The iTS, rLN, high risk factor and intermediate risk factor were significant prognostic factors on univariate analysis for both OS and PFS, but were not significant on multivariate analysis. Among the patients who had no or one postoperative risk factor and did not receive the adjuvant therapy (n=27), no recurrences or deaths were reported even though 13 patients had one or more pretreatment risk factors.

Conclusions: In the setting of NACT plus surgery for cervical cancer, several clinicopathological factors showed potential relationship with clinical outcomes, but there were no independent prognostic factors. Adjuvant radiotherapy may not be required in patients without enough postoperative risk factors regardless of the presence of pretreatment factors.
Poster Session II

INTEGRATION OF ANGIOGENIC MARKER AND MOLECULAR IMAGE FOR DETERMINATION OF PROGNOSIS IN CERVICAL CANCER

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Objectives: Endoglin and TGF-β1 are considered as key factors for tumor angiogenesis. We attempted to investigate the correlation between endoglin/TGF-β1 expressions and survival. We also evaluated the possibility of using diffusion-weighted MRI (DW-MRI) and serum endoglin levels for noninvasive measurement of angiogenesis.

Methods: We retrospectively analyzed endoglin microvessel density (MVD) and TGF-β1 IHC expression from 80 patients of cervical cancer before CCRT. Survival of these patients with different endoglin and TGF-β1 IHC expressions were analyzed. In vitro, HUVECs were cultured with different TGF-β1 concentration and duration. Expressions of endoglin were then determined by Western blotting. Another 32 patients were examined prospectively using DW-MRI and values of apparent diffusion coefficient (ADC) were collected. Serum levels of endoglin and tumor MVD were also quantified from these 32 patients prior to CCRT.

Results: The optimal cutoff value of endoglin MVD in predicting survival was 11.125. Strong TGF-β1 with high MVD was significantly associated with poor survival. Our in vitro results showed that expressions of endoglin were up-regulated as TGF-β1 concentration or duration increased. When compared with normal controls, serum endoglin levels were significantly elevated in cervical cancer patients and correlated well with tumor size and tissue endoglin MVD. Correlation was also seen between ADC values and endoglin expression.

Conclusions: Our results suggested that TGF-β1 may act as a promoter of tumor angiogenesis. The ADC values on DW-MRI are influenced by tumor angiogenesis, as reflected by increased endoglin expression. Therefore, DW-MRI and serum endoglin determination are potential noninvasive procedures for assessing tumor angiogenic activity.
Poster Session II

POST-OPERATIVE TAXANE-PLANTINUM THERAPY IMPROVES OVERALL SURVIVAL IN NEUROENDOCRINE CERVICAL CARCINOMA

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Background and objective: Neuroendocrine cervical carcinoma (NECC) is a rare malignancy, accounting for less than 5% of all cervical cancers. NECC is highly aggressive, with an early lymphatic dissemination and a high rate of distant recurrences, and has a high mortality. The aim of this study was to see whether taxane-plantinum therapy after surgery can improve overall survival in NECC.

Methods: Twenty-one women with International Federation of Gynecology and Obstetrics (FIGO) early stage Ia2 (n=1), Ib1 (n=19), and Ib2 (n=1) were treated with surgery, followed by post-operative taxane-plantinum or other chemotherapy, with or without radiotherapy, in our hospital between 2004 and 2011. Medical charts were retrospectively reviewed and clinical data retrieved. The Kaplan-Meier method, log-rank test, and the Cox regression model were used for survival analysis.

Results: The 21 patients had a median age of 40 years (range: 25—63). The overall 2-year survival rate was 56.8% (95% confidence interval (CI): 36.6%—88.1%). Lymphovascular space invasion was seen in 15 patients (71.4%). Seven (33.3%) had lymph node metastases, and 4 (19.0%) had parametrial infiltration. Thirteen patients received post-operative taxane-plantinum therapy or other chemotherapy, with or without radiotherapy, in our hospital between 2004 and 2011. Medical charts were retrospectively reviewed and clinical data retrieved. The Kaplan-Meier method, log-rank test, and the Cox regression model were used for survival analysis.

Conclusion: NECC is a deadly variant of cervical cancer. Postoperative taxane-plantinum therapy appears to significantly improve the overall survival with NECC.
A PROSPECTIVE STUDY OF ANORECTAL MANOMETRY FOR THE ASSESSMENT OF ANORECTAL DISABILITIES FOLLOWING RADICAL HYSERECTOMY IN PATIENTS WITH CERVICAL CARCINOMA


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Aim of this study: To objectively assess anorectal function following radical hysterectomy in early stage cervical carcinoma patients.

Material and methods: From January 2008 until December 2008, 21 patients with primary cervical cancer stage FIGO I-II were enrolled in this prospective study.

All women underwent class III radical hysterectomy according to Piver-Rutledge classification, with or without neoadjuvant chemotherapy and adjuvant radiotherapy.

Anorectal manometry was performed preoperatively and 1 year after surgery. The following parameters were assessed: maximum and mean resting sphincter pressure, maximum and mean squeeze pressure, anal area at rest, anal area in squeezing, length of high pressure zone, recto-anal inhibitory reflex (RIRA), RIRA threshold, RIRA latency, sphincter pressure decrease during RIRA, RIRA duration, length of high pressure zone, threshold perception of distension, threshold of perception of the evacuative stimulus, maximum tolerated volume and rectal compliance.

Preoperative and postoperative data were compared with student t-test considering significative p value < 0.05. Patients were also divided into subgroups whether or not they had received neoadjuvant chemotherapy or adjuvant radiotherapy, a student t-test was then used to compare the manometric evaluations in each group.

Results: No statistically significative differences were found when comparing each preoperative and postoperative anorectal manometric parameters. No differences were found neither when dividing the same patients in groups whether or not they underwent chemotherapy or radiotherapy.

Conclusion: Our findings suggest that class III radical hysterectomy does not seem to be associated with long term anorectal dysfunction in patients with early stage cervical cancer.
Poster Session II

CERVICAL CANCER TREATMENT FOR OPERABLE LESIONS IN A LOW-RESOURCE CONTEMPORARY SETTING

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**Background:** To compare HIV+ and HIV- women with operable cervical cancer in a low resource contemporary setting.

**Methods:** A retrospective study using well-matched controls from a Kenyan teaching and referral hospital.

**Results:** 183 women were treated for cervical cancer between October 2007 and June 2011. At presentation, 28 had operable lesions (Stage IA1-IIB1); 7 received neoadjuvant chemo prior to surgery. HIV seroprevalence was 54%(18/33) among initial operative cases and 57% among the neoadjuvant group (p=ns). Mean age was 42(HIV+), and 43(HIV-), (range 25-64). HIV- vs. HIV+ cervical cancer patients (mean CD4 count 373, 50%< 200) were detected by visual inspection with acetic acid (VIA) (18%(2/11) vs. 68%(15/22) p=.099), symptoms (27%(3/11) vs 14%(3/22) p=.43), or Pap smear (45%(5/11) vs 09%(2/22)[CL1] ) p=.06), respectively. HIV+ patients (two Stage IB1, two Stage IB2) did not require more downstaging than HIV- patients (two stage IIb, one stage IIIA) before surgery (18%,(4/22) vs 27%(3/11)[CL2] p=.63). Surgical treatments were not statistically different in either group. Immediate postoperative complications included fever, dehiscence, DVT, ileus, fistula, and infection. One HIV- patient suffered immediate postoperative fever, vesicovaginal fistula, and wound dehiscence (overall complications 6%). Lymph node involvement was noted in 7 HIV+ and 3 HIV- patients who underwent full staging procedures (p=.004).

**Conclusions:** In patients with operable cervical cancer, HIV serostatus does not affect complication rate or influence need for downstaging prior to surgery compared to a well-matched control group. HIV+ patients were not more likely to receive neoadjuvant chemotherapy but were more likely to have positive lymph nodes.
Poster Session II

SPATIAL ANALYSIS OF CELL PROLIFERATION, P16 EXPRESSION, NUCLEAR MORPHOMETRY AND PATHOLOGY IN 53 LEEP CERVICAL SPECIMENS

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The architectural complexity of multiple CINs and HPV infection in cervical epithelium is still poorly understood. Our objective was to study quantitatively the spatial correlation between HPV infection, cell proliferation and Tissue Phenotype of cervical epithelium. Women scheduled for colposcopy and loop electrosurgical excision procedure (LEEP) treatment at the VGH Women's Clinic were recruited for participation in this study. So far 53 LEEP specimens for about 30 sections each were processed and reviewed. Two additional sections were stained on 13 specimens; one was stained for the dual expression of p16INK4a and Ki-67; and one with Feulgen stain for Quantitative Tissue Phenotype analysis. All sections were scanned at 40X using a Whole Slide Scanner. Exhaustive reviews and selection of all individual areas of CIN were performed on the H&E sections and the matching areas on the other two stained sections were analyzed using our in house imaging software Getafics, for tissue architecture, cell sociology and nuclear morphology analysis.

So far, four patients have been diagnosed with no CIN lesions, 4 have been diagnosed with CIN I lesions, 6 have been diagnosed as CIN2 (6 of them with CIN1 and CIN2 lesions); 37 have been diagnosed as CIN III; among them, only 4 had only CIN3 lesions whereas 3 showed CIN1 and CIN2 lesions, 10 showed CIN2 and CIN3 lesions and 20 showed CIN1, CIN2 and CIN3 lesions.

We will present the results of our quantitative spatial correlations within each section, within each LEEP specimens and between the different stains.
Poster Session II

CONCOMITANT OXALIPLATIN AND RADIATION RESULTS IN HIGHER GROWTH INHIBITION IN CERVICAL CANCER CELL LINES COMPARED TO CISPLATIN AND RADIATION

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Objective: To compare the sensitivity of cervical cancer cell lines to the combination of radiation and oxaliplatin versus radiation and cisplatin using an in-vitro assay.

Methods: Four cervical cancer cell lines (C33A, CaSki, ME180 and SiHa) were exposed to ionizing radiation with and without oxaliplatin or cisplatin, upon which tetrazolium (XTT) proliferation assay was analyzed. Results were reported as the fraction of proliferation compared to control. The data was analyzed using the median effects principle of Chou and Talalay where a combination index < 0.9 indicated synergism. Expression of p53 and hMSH2 was studied.

Results: Radiation dose-dependent proliferation was observed for all cell lines (Figure 1,2). High risk (HR) HPV+ (CaSki and SiHa) cells were more resistant to radiation, cisplatin and oxaliplatin. The mean combination index values at doses close to half maximal inhibitory concentration (IC-50) suggested higher synergistic effects with combination of oxaliplatin and radiation compared to cisplatin and radiation in ME 180, SiHa, and Caski cell lines (Table 1). Decreased p53 and hMSH2 expression correlated with HPV 16 and 18 expression in CaSki and SiHa cells and the pattern of response to chemotherapy and radiation.

Conclusions: In HR-HPV+ cervical cancer cell lines, concomitant oxaliplatin and radiotherapy results in higher level of growth inhibition compared to cisplatin and radiotherapy. Defects in mismatch repair pathway may confer resistance to radiation and cisplatin treatment but not to combination of oxaliplatin and radiation. This effect and the more favorable toxicity profile of oxaliplatin, makes it an attractive radio-sensitizer in management of cervical cancer.
Poster Session II

VASCULAR ENDOTHelial GROWTH FACTOR (VEGF) EXPRESSION IN CERVICAL INTRAEPITHELIAL NEOPLASIA AND CERVICAL CANCER


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Background: Neoangiogenesis represent a process of building a new vascular net which provides tumour growth, infiltration and metastasis.

Methodology: The expression of VEGF was examined and compared in the cervical tissue in 109 patients divided into three groups: the control group: 30 patients (normal cervix), group A: 33 patients (H SIL lesions) and group B: 46 patients (cervical cancer, FIGO st. IB). The VEGF expression was analysed and compared with histopathological parameters in group B. The correlation among groups and subgroups was also analysed.

Results: The expression of VEGF was not confirmed in the control group. In group A and group B, VEGF expression was found in, 33.33% vs. 60.87%, p< 0.05. The high level of expression of VEGF expression was confirmed in A-3% vs. B-30.4%, p=0.0016. There was no statistically significant difference in the level or expression of VEGF in group A regarding the type of intraepithelial lesion, neither in group B regarding the histopathological parameters. In patients with poor histopathological prognostic parameters such as tumour diameter larger than 2 cm (24/46), depth of the stromal infiltration larger than 10 mm (32/46), positive lymph nodes (17/46) and with infiltration of the uterine body (11/46) a statistically significant difference was confirmed regarding the expression of VEGF (p< 0.05).

Discussion and conclusion: Frequent expression of VEGF in group of patients with HSIL and cervical cancer indicates the importance of VEGF as a proangiogenic factor in carcinogenesis of cervical cancer. A further investigation could be aimed at the investigation of this marker as prognostic factors in the high risk group of patients with cervical cancer.
Poster Session II

CYCLOOXYGENASE-2 EXPRESSION IN CERVICAL CANCER

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Background: COX-2 expression was a significant factor in the increase of the tumor angiogenesis and the reduction of apoptosis, which appeared as a possible, important connection within the development of carcinogenesis and the tumor growth.

Objective: The expression level of COX-2 was compared in patients with cervical cancer in relation to the degree of tumor differentiation, stromal invasion, tumor size, presence of lymphovascular invasion and existence of metastases in the lymph nodes and control group with no cervical pathology.

Material and methods: The study included histological material of 76 patients divided into two groups: the control group - 30 patients without histopathological changes in the cervix and the group A - 46 patients with verified cervical cancer, FIGO stage IB-IIA. Histopathological and immunohistochemical analysis were performed in these two groups of patients.

Results: In the control group, the expression of COX-2 was not confirmed, while in the group A, it was confirmed in 26 patients (56.52%). The expression of COX-2 was more pronounced in the stromal tissue without lymphocytic infiltration, 80% vs. 20%, p = 0.0053. In a subgroup of patients with worse histopathological prognostic parameters such as positive lymph nodes (17/46), lymphovascular infiltration (18/46), infiltration “isthmus” of uterus (11/46), expression of COX-2 was 70.59%, 66.66%, 63.54%.

Conclusion: COX-2 expression in the group with cervical cancer compared to the control group points to the potential impact of COX-2 in carcinogenesis of cervical cancer. The expression of COX-2 was higher in cervical carcinoma without stromal lymphocytic infiltration suggesting a possible paradoxical effect of COX-2 in immunosuppression in tumor tissue. The finding of frequent COX-2 expression in the subgroup with poor prognostic histological parameters in the group A indicates the importance of the COX-2 expression in the carcinogenesis of cervical cancer.
Poster Session II

REHABILITATION OF ENDOMETRIAL AND CERVICAL CANCER PATIENTS: A STUDY OF NEEDS AND PRIORITIES

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Aim: Identifying short-term rehabilitation needs of women newly diagnosed with cervical or endometrial cancer.

Methods: Recruitment was performed consecutively in a six month period from September 2011. A questionnaire was completed pre-treatment and three months later. Questionnaires used were: The European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire (EORTC QLQ-C30), either the Cervix Cancer (QLQ-CX24) or the Endometrial Cancer module (QLQ-EN24), and the Three-Levels-of-Needs Questionnaire (3LNQ). The Wilcoxon signed rank test evaluated the results statistically.

Furthermore, randomly selected women from the questionnaire group were invited to participate in one of two qualitative focus groups.

Results: 98 women were included in the study and 52 have so far reached the three month questionnaire. Analysis of the 52 completed patients showed a high level of depression and worry pre-treatment. However, after three months the emotional functioning improved (p = 0.0001) and the burden due to depression and worry decreased (p = 0.003). Unmet need of help with worries was reported in 41% and both focus group interviews confirmed this finding qualitatively. Compared with pre-treatment scores, endometrial cancer patients reported more gastrointestinal (p = 0.003) and urogenital symptoms (p = 0.008) three months later, while cervical cancer patients reported more sexual/vaginal problems (p = 0.06). 23 % reported an unmet need of help with sexual functioning and qualitative findings suggested the importance of discussing sexual matters.

Conclusions: Pre-treatment rehabilitation efforts should focus on emotional and psychological functioning, whereas attention should be directed to physical side-effects after treatment.
Poster Session II

ADVERSE OBSTETRICAL OUTCOMES ASSOCIATED WITH TREATMENT FOR CERVICAL INTRAEPITHELIAL NEOPLASIA

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Objective: The objective of this study was to quantify the relationship between adverse obstetrical outcomes and cervical excisional procedures (CEP) [cold knife conization, loop electrosurgical procedure, cryotherapy, laser conization and ablation] as treatment for CIN.

Study methods: ICES databases containing information on health care utilization were analyzed for the period January 1, 1992 until March 31, 2010. An inception cohort of women with one or more deliveries following exposure to CEP was compared to women referred to colposcopy with a cytologic abnormality not exposed to a CEP. Logistic regression analysis was undertaken to determine odd ratios for adverse outcomes.

Result: For the periods under study, 381617 women were eligible for study inclusion, of which 180586 had a delivery. A total of 12,533 women underwent a CEP compared to 14,502 in our comparison cohort - women exposed to colposcopy but no CEP. Distribution of ages at inception was 13 to 19, and follow-up data was available up to age 37. Cohorts were similarly distributed according to age at first delivery, chronic disease status, urban versus rural distribution and socioeconomic status. Of all CEP, 63.3% occurred by age 25. A CEP increased the risk of cervical incompetence (OR 2.55 p< 0.01), PROM (OR 1.25 p< 0.01), preterm birth (OR 1.46 p< 0.01) and risk of cervical stenosis in a subsequent pregnancy (OR 3 p< 0.01).

Conclusion: Cervical excisional procedures increase the risk of adverse obstetrical outcomes. Caution must be taken to avoid overtreatment in young women with mild CIN.
Poster Session II

THE MANAGEMENT OF NEUROENDOCRINE SMALL CELL CARCINOMA OF CERVIX IN NORTHERN IRELAND OVER A TEN YEAR PERIOD

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Purpose: To determine disease free and overall survival of neuroendocrine small cell cancer of cervix treated at the Northern Ireland Cancer centre between 1999 and 2010.

Materials and methods: A retrospective review of all patients diagnosed and treated with neuroendocrine small cell cancer of cervix in Northern Ireland. Details of treatment modality including chemotherapy, radiotherapy and surgery were recorded.

Results: 15 patients diagnosed with neuroendocrine small cell carcinoma (NSCC) of cervix were identified between 1999 and 2010, 12 with disease localised to the pelvis and 3 with metastatic disease. 3 year overall survival for all patients was 65% and disease free survival was 45% for all patients. In patients with pelvic confined disease 3 year overall survival was 79% and disease free survival was 57%. Median disease free and overall survival is 30 and 39.6 months respectively. These survival rates compare very favourably to those reported in the literature. Stage of disease at diagnosis was the main determinant of survival.

Conclusion: Local control and survival can be achieved in NSCC of patients with a combination of irradiation and platinum-based chemotherapy. Stage of disease determines outcomes.
Poster Session II

ASSOCIATIONS BETWEEN PAPANICOLAOU TESTING AND CERVICAL CANCER IN ELDERLY WOMEN

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Objectives: To determine whether Pap testing after age 65 is associated with the incidence of subsequent cervical cancer.

Methods: The SEER-Medicare database was used to identify women diagnosed with cervical cancer after age 70 from 1992-2007. Cases with complete billing data, totaling 734 women, were matched in a 1:4 ratio with 2,936 controls from a 5% random sample of non-cancer Medicare patients. In addition, a subgroup of 126 cervical cancer cases with at least one Pap test between ages 65-70 was separately matched with similarly tested controls in a 1:4 ratio. Separate conditional logistic regression analyses were performed to assess 1) the utility of cervical cancer screening between ages 65-70, and 2) the utility of additional testing after age 70.

Results: Overall, 17.3% of cases received a Pap test between ages 65-70, compared to 24.6% of controls, which was a statistically significant difference (OR 0.62, 95% CI 0.50 - 0.77). In the subgroup analysis of patients with at least one Pap test between ages 65-70, no association was identified between Pap testing after the age of 70 and subsequent diagnosis of cervical cancer (OR 1.51, 95% CI 0.97 - 2.33).

Conclusion: This study demonstrated an association between Pap testing done from ages 65-70 and a decreased incidence of cervical cancer. Among women with a Pap test between 65-70, however, no association was identified between subsequent testing and cancer incidence, which suggests that additional Pap testing among previously tested women after age 70 may lack protective benefit.
Poster Session II

CERVICAL CANCER INCIDENCE AND SCREENING PATTERNS IN ELDERLY WOMEN

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Objectives: To determine whether the incidence of cervical cancer among Medicare enrollees changed from 1992-2007, and whether this was associated with changes in Pap testing or colposcopy.

Methods: The SEER-Medicare database was used to identify women diagnosed with cervical cancer at ages 65+, as well as rates of cancer incidence based on the number of similar women at risk. Medicare billing data for a random 5% sample of non-cancer patients was used to identify rates of Pap testing and colposcopy. Generalized linear models with a Poisson error distribution were used to determine trends in these respective rates.

Results: SEER data identified 6,718 women who met our criteria. Cervical cancer rates decreased from 1.19 cases per 10,000 women in 1992 to 1.008 cases per 10,000 in 2007. While the incidence of stage I cancers decreased by 2.4% (95% CI 1.5%-3.3%, p < 0.0001) per year, the incidence of stage III disease increased by 2.0% (95% CI 1.0%-4.0%, p=0.0002) per year. Annual rates of colposcopy decreased by 3.7% per year (95% CI 3.2%-4.1%, p< 0.0001) and rates of Pap tests decreased by 1.3% per year (95% CI 1.3%-1.4%, p< 0.0001).

Conclusions: The incidence of stage I cervical cancer in elderly women has decreased, which may be explained by the cohort effect of routine screening over the last 30 years. The contrasting increase in stage III cancer could be related to decreases in Pap testing and colposcopy, or could be due to other factors such as an increase in biologically aggressive disease.
Poster Session II

PREDICTING PARAORTIC NODE (PAN) RECURRENCE OF CERVICAL CANCER AFTER RADICAL HYSTERECTOMY (RH): INDICATIONS FOR TREATMENT OF PAN AFTER RH

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Objective: In the Japanese Guideline for managing cervical cancer, the significance of paraaortic node (PAN) dissection/biopsy during radical hysterectomy (RH) and PAN radiotherapy are described, but the indications are subobsolete. The US guideline recommends postoperative PAN irradiation if surgical staging confirms PAN metastasis pathologically. In this study, risk factors for PAN recurrence after RH were reviewed to allow prediction of PAN metastasis preoperatively or intraoperatively.

Methods: We reviewed 35 patients with first recurrence of the PAN (initial PAN recurrence) among 828 patients undergoing RH (1994–) and found that 31 patients (88.6%) were pN1. Therefore, we analyzed risk factors for PAN recurrence in 218 pN1 patients. We excluded patients with preoperative chemotherapy, PAN dissection/biopsy, Extended field radiotherapy, and < 10 nodes harvested by pelvic lymph node dissection, from 218 pN1 patients. All patients had squamous cell carcinoma, adenocarcinoma, or adenosquamous cell carcinoma.

Results: Among 113 pN1 patients, 69 had no recurrence, 16 had initial PAN, and 28 had recurrence without PAN metastasis. The number of metastatic pelvic lymph nodes showed a significant difference between patients with initial PAN recurrence and patients without recurrence (p< 0.05). Multivariate analysis revealed that extention to the corpus (p< 0.05) and >2 metastatic pelvic lymph nodes (p< 0.01) were significant risk factors for initial PAN recurrence in pN1 patients undergoing RH.

Conclusions: When pelvic lymph node metastasis is confirmed, and extention to the corpus or >2 metastatic pelvic nodes are observed during RH, additional PAN treatment (dissection or radiotherapy) should be performed.
Poster Session II

RADICAL VAGINAL TRACHELECTOMY- SIGNIFICANCE OF THE LOWER UTERINE SEGMENT PRESENCE IN THE SUPERIOR MARGIN OF THE PATHOLOGIC SPECIMEN

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Objective: To report if the presence of lower uterine segment (LUS) in the superior margin of the pathological trachelectomy specimen is associated with preterm birth following vaginal radical trachelectomy (VRT) for early-stage cervical cancer.

Methods: Review of 143 prospectively recorded patients treated by a laparoscopic pelvic lymphadenectomy (PLN) and VRT from January 2000 to December 2011 with regards to their cervical pathology and reproductive outcomes. Pathology was re-reviewed to identify the presence of LUS in the superior surgical margin.

Results: The median age was 31.5 years old, and 66% were nulliparous at time of surgery. Stage distribution was; 1A1 (14%), 1A2 (29%), and 1B1 (57%). No adjuvant treatment was administered to 90.1% of the patients. 52 pregnancies occurred, of which 30 (58%) reached the third trimester. The presence of the LUS in the superior surgical margin was identified in 60 patients (42%). When the groups were compared based on the absence or presence of LUS: 77% vs. 70% of the patients reported attempted conception and 43% vs. 27% were successful respectfully. The incidence of a gestation greater than 24 weeks was 37% vs. 20% (OR=0.42 [95% CI 0.19-0.92], p=0.03) and the term pregnancy incidence was 27% vs. 20% (OR=0.37 [95% CI 0.15-0.92], p=0.03) in favor of the patients without LUS.

Conclusions: The presence of LUS in the superior margin of the trachelectomy specimen is associated with a higher likelihood of preterm birth.
Poster Session II

RADICAL VAGINAL TRACHELECTOMY: FERTILITY OUTCOMES AND SIGNIFICANCE OF LOWER UTERINE SEGMENT PRESENCE IN THE SUPERIOR MARGIN OF THE PATHOLOGIC SPECIMEN

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Conclusions: The presence of LUS in the superior margin of the trachelectomy specimen is associated with a higher likelihood of preterm birth.
Poster Session II

A CORRELATION BETWEEN CYTOLOGY AND COLPOSCOPY DIRECTED BIOPSY IN CASES WITH ATYPICAL SQUAMOUS CELL WITH UNDETERMINED SIGNIFICANCE

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Objective: The aim of this study was to determine the correlation between cytologic diagnosis of ASC-US with colposcopy directed biopsy findings.

Materials and methods: 110 women with cytologic diagnosis of ASC-US were selected and followed by colposcopic examination and cervical biopsy.

Results: 99 women had normal colposcopic findings. Biopsy showed normal finding in 89 cases and koilocytosis in 10 cases.

11 cases had abnormal colposcopy and biopsy showed HPV infection in 7 cases, LSIL in 2 cases, HSIL in one case and squamous cell carcinoma in one case.

Conclusion: The women with cytological finding of ASC-US and normal colposcopy are unlikely to have high grade lesion in final pathology.
INDUCTION CHEMOTHERAPY FOLLOWED BY CONCURRENT CHEMORADIATION WITH PACLITAXEL PLUS CISPLATIN FOR CERVICAL CANCER WITH COMMON ILIAC AND/OR PARA-AORTIC NODE ENLARGEMENT

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Objectives: The aim of this study was to evaluate the efficacy of induction chemotherapy using paclitaxel plus cisplatin (TP-ICT) followed by concurrent chemoradiotherapy with TP (TP-CCRT) in cervical cancer with common iliac (COM) and/or para-aortic node (PAN) enlargement.

Methods: Between April 2008 and December 2011, 22 patients with cervical cancer (CC) were enrolled. Treatment consisted of two 21-day cycles of cisplatin 50 mg/m² and paclitaxel 175 mg/m² intravenously followed by 2 to three 21-day cycles of cisplatin 50 mg/m² on day 1 and paclitaxel 50 mg/m² on days 1, 8 and 15, with CCRT of extended field and high-dose rate intracavitary brachytherapy. Only patients who achieved CR, PR or SD with TP-ICT proceeded to TP-CCRT. Overall survival (OS), disease-free survival (DFS), central disease-free survival (CDFS), distant disease-free survival (DDFS) were estimated in comparison with historical controls treated CCRT using cisplatin alone (P-CCRT).

Results: The objective response rate was 90.9% (CR,1; PR,19; SD,1; PD,1) after TP-ICT. Of 21 patients who achieved CR, PR, or SD by TP-ICT, 18 patients showed CR after TP-CCRT. After a median follow-up of 22 months, 15 patients are free from disease, 3 alive with disease, and 4 died of the disease. OS, DFS, and DDFS in study group were superior to those in historical controls group (p=0.037, p=0.021, and p=0.026, respectively). There was not statistic difference in those groups for CDFS. Acute and late adverse effect were acceptable.

Conclusions: TP-ICT followed by TP-CCRT showed a promising activity in CC with COM and/or PAN enlargement.
Poster Session II

INVASIVE ROLE OF TGF-BETA IN UTERINE CERVICAL CANCER

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We do not have a good agent to treat advanced uterine cervical cancer, besides operation, radiotherapy, and chemotherapy. In uterine cervical cancer, transforming growth factor beta (TGF-beta) is known as a tumor suppressor, but its tumorigenic role has seldom discussed. We have investigated its tumorigenic role through immunohistochemistry, and western blotting of phosphorylated Smad3 (pSmad3), representing activation of TGF-beta, and invasion assay. Immunohistochemistry showed pSmad3 staining in boundary areas of cancer lesions which were adjacent to normal stroma. Western blotting showed expression of pSmad3 in cervical cancer lineage, CaSki, after treatment of TGF-beta. Invasion assay showed that significantly more cells with TGF-beta invaded than cells without TGF-beta (p=0.0114), and that significantly less cells with both TGF-beta and its inhibitor, A83-01, invaded than cells with only TGF-beta (p=0.0135). These results suggested that TGF-beta may have a potential to work in cancer invasion and that TGF-beta signaling may become a target of treatment of uterine cervical cancer.
Poster Session II

CLINICAL ANATOMY OF FIGO STAGE 2B CERVIX CANCER; PATTERNS OF FAILURE AND SURVIVAL

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Purpose: To observe the extent of tumour in FIGO stage 2b cervix cancer and to study the prognostic significance of these for patterns of failure and survival.

Methods: One hundred and fifty-seven, 2b cervix cancer patients, following clinical staging were treated with chemoradiotherapy between 1996 - 2008. MRI and PET were used to assess the tumour volume, corpus invasion, parametrial extension and nodal spread. Nodal metastasis received an additional dose of 6-10Gy following 40Gy to whole pelvis. Brachytherapy boost of 40 Gy (EQD=2) was applied to primary tumour. Staging, treatment and follow-up data were collected prospectively. Potential prognostic factors were examined in relation to patterns of failure and survival.

Results:

<table>
<thead>
<tr>
<th>Parametrial Categories</th>
<th>Not involved %</th>
<th>Unilateral %</th>
<th>Bilateral %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parametrial status</td>
<td>26</td>
<td>42</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Median Tumor Volume cc</td>
<td>27</td>
<td>41</td>
<td>50</td>
<td>0.035</td>
</tr>
<tr>
<td>Corpus invasion</td>
<td>56</td>
<td>74</td>
<td>84</td>
<td>0.014</td>
</tr>
<tr>
<td>PET + nodes</td>
<td>39</td>
<td>33</td>
<td>49</td>
<td>0.352</td>
</tr>
</tbody>
</table>

Multivariate model showed, presence of nodal metastasis and adenocarcinoma histology for FFS and OS and corpus invasion was significantly associated with FFS only.

Relapse rate was 36%. Pelvic and primary site relapse was 16% and 12%. Only 8 (5%) patients failed exclusively in pelvis. One patient suffered isolated primary relapse, was successfully salvaged by hysterectomy.

Conclusion: In FIGO stage 2b cervix cancer, treated by chemo-radiotherapy, the absence or presence of parametrial invasion played no significant prognostic role once the corpus invasion and nodal status in these patients was known.
Poster Session II

LAPAROSCOPIC ASSISTED PELVIC EXENTERATION - LIGHT AT THE END OF THE TUNNEL

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Background, aims and objectives: Locally advanced cervical cancer (LACC) remains a therapeutic challenge. Laparoscopic Assisted Pelvic Exenteration (LAPE) may pave the way to reduce the morbidity of extensive open surgery while facilitating easy dissection. This retrospective study aims to describe our immediate results of LAPE for LACC.

Methods: The study retrospectively analysed data of 15 patients who underwent LAPE (8 anterior, 6 total, 1 inoperable) in a single unit at our hospital (08/2010 to 03/2012). All patients received prior chemoradiotherapy, 3 patients had recurrence post surgery/chemo-radiation. Exenteration surgery with curative intent was attempted after laparoscopic trial dissection. Urinary diversion was achieved by ileal conduit or wet colostomies.

Results: 1 patient was inoperable (rectosigmoid deposits), 5 had total laparoscopic exenteration, and 9 patients had laparoscopic assisted exenteration. Extensive pelvic disease mandating extended pelvic exenteration (4 patients), need to achieve R0 resection, time constraints and bleeding were reasons for conversion. Mortality at 30 days was nil, ninety days was 2 (13%) (1 Burst abdomen, 1 severe sepsis), major morbidity was seen in 6 patients (40%) (sepsis, infections) Minor morbidities (electrolyte imbalances, hypoproteinemia) were seen in 13 patients (86.6%). Immediate postoperative outcome correlated with poor preoperative nutrition status and socio economic status.

Conclusion: LAPE has an acceptable immediate postoperative outcome. Laparoscopy gives an added advantage of reducing the morbidity and easier dissection of the lateral pelvic wall. Conversion, however, may be necessary to achieve R0 resection in selected patients. Pre and post operative nutrition is important for a good result.
Poster Session II

OVARIAN TISSUE CRYOCONSERVATION IN PATIENTS WITH GYNECOLOGICAL MALIGNANCIES

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During recent years the increase incidence rate of gynecological malignancies in reproductive age patients who had no time to implement generation function has been registered. In majority cases special treatment results in partial or full deprivation of fertility as a result of the high ovarian sensitivity to chemotherapy and radiation therapy. Cryopreservation and autotransplantation of ovarian tissue appear to become the method of fertility preservation.

The aim of the work was to evaluate the ovarian reserve and develop policy of treatment in patients with gynecology malignancies with the purpose of cryoconservation of ovarian tissue for further realization of reproductive function.

8 patients of reproductive age (< 35 years) have been treated in National Cancer Institute from 2010 to 2012 year with diagnosis IB - IIB stage cervix cancer. Panhysterectomy type 3 has been executed in 7 patients, radical abdominal trachelectomy - in 1 patient. Ovarian tissue obtained after laparotomy was placed in aseptic terms in container with special medium with temperature +20-25 ° C and after that it was transported to Institute of Cell Therapy for following investigation, cryopreservation and further preservation. Currently all the patients are placed under dynamic surveillance. There is no evidence of the disease.

As a result cryoconservation of ovarian tissue can be fulfilled with the aim to realize the delayed reproductive function. This method does not require the delay of the treatment, ovarian stimulation and can be accepted for the patients with gynecological malignancies.
Poster Session II

URINE HUMAN PAPILOMA VIRUS PREVALENCE IN WOMEN WITH HIGH-GRADE CERVICAL LESIONS

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Background: Cervical cancer screening has drastically reduced the incidence. In Spain only 75% of women keep adequate gynecologic controls. In fact, 80% of cervical cancer cases occur in wrong-screened population. Previous studies have suggested an association between high-grade cervical lesions and positive HPV in urine samples. Sensitivity and specificity obtained in urine samples have been shown lower than those from cervical swabs, therefore urine HPV detection should not replace the traditional screening method, but could be considered as an alternative method if the prevalence was high.

Materials and methods: 76 women with a positive biopsy for CIN2+ were included in the study from October 2010 to July 2011, and a sample of urine was collected immediately before a conization at the outpatient clinic. We analyze the presence of HPV using a PCR-based technique.

Results: The mean age was 34.8 years. All patients had histological CIN2+, of whom 40.1% had CIN3+. The prevalence of HPV in urine test was 68% in CIN2+ population versus 71% in CIN3+ patients. The most current HPV genotype was 16-HPV, which was located in 58% of women with positive HPV-DNA in urine samples. Smoking status, parity and 16 HPV genotype were found to significantly associate to urine HPV prevalence.

Conclusions: The prevalence of HPV in urine samples in patients with CIN2+ was 68%. HPV-DNA urine detection could be considered for high-risk population who skip regular programs. We aim to start a cohort study based on high-risk population to test this hypothesis.
ASSOCIATION BETWEEN CERVICAL HPV STATUS AND VAGINAL PH

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Objectives: The aim of the study was to find out the relationship between cervical HPV status and vaginal pH.

Patients and methods: The study comprised of 320 women aged 18-67 at enrollment visiting our oncology outpatient department with a PAP smear finding of squamous intraepithelial lesions. HPV was sampled from the cervical mucus and polymerase chain reaction was used for HPV detection and typing. Vaginal pH was evaluated using Merck's vaginal pH strips. Results were stratified by age at visit.

Results: HPV was positively associated with vaginal pH, mainly in women younger than 35 years. Vaginal pH higher than 4.5 was associated with 34% greater risk of infection with multiple HPV types, especially in women younger than 35 years and women older than 60 years. (OR 2.3 95% CI).

Conclusions: The results suggest eventual association of the cervical and vaginal microenvironment influencing the HPV natural history and cervical cancer development. Larger study, including identification of the cervicovaginal microbiome is necessary for more detailed data.
Poster Session II

CHANGE OF CHEMOSENSITIVITY OF CERVICAL CANCER CELL LINES BY RNA INTERFERENCE TO HPV16 E6

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Objective: To explore the effect of HPV16 E6 siRNA to the chemosensitivity of cervical cancer cell lines (Caski and SiHa).

Methods: Chemosensitivity of Caski and SiHa cell lines were checked by MTT method using cisplatin (DDP), 5-fluorouracil (5-FU), bleomycin (BLM) before and after HPV16 E6 siRNA transfection which was encapsuled by virus plasmid. Cell lines were cultivated with above medications at 10 times, 5 times, 1 time, and 0.1 time concentration of peak plasma level. The expressions of P53 and caspase-3 proteins were also assessed by flowcytometry (FCM) before and after siRNA transfection.

Results: The chemosensitivities of both cell lines were dose and time dependant before and after siRNA transfection, which were statistically different among various doses and culcure time (P< 0.05). The expressions of P53 and caspase-3 proteins in both cell lines were increased markedly after HPV16 E6 siRNA transfection, especially for Caski cell line (P< 0.05). The apoptosis of both cell lines were increased significantly after HPV16 E6 siRNA transfection even at low levels of medication concentrations compared with high level concentration (P< 0.05).

Conclusion: HPV16 E6 siRNA can effectively restrain the proliferation of Caski and SiHa cell lines, increase the chemosensitivity of chemotherapy and the expressions of caspase-3 and p53 protein. RNA interference to HPV could help to overcome the chemoresistance in some chemotherapy regimens.
Poster Session II

RETROSPECTIVE ANALYSIS: PATIENT WITH LOW & INTERMEDIATE GOG RISK SCORE FOLLOWING RADICAL HYSTERECTOMY & PELVIC LYMPHADENECTOMY IN EARLY CERVICAL CANCER

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Objective: Adjuvant treatment post radical hysterectomy for early cervical cancer, nodal negative varies among centers. Gynecology Oncology Group (GOG) score categorized these patients into low, intermediate and high risk based on lymphovascular invasion, deep stromal involvement and tumor size. We aimed to evaluate the outcomes for low and intermediate GOG score treated in our center.

Methods: Sixty three patients with early stage cervical cancer, nodal negative after radical hysterectomy and pelvic lymphadenectomy between 2004 and 2009 were retrospectively analyzed. The GOG score proposed by Delgado et al was applied and patients were stratified into three groups; low(< 40), intermediate(40-120) and high(>120). Only patients with high GOG score had post operative adjuvant chemoradiotherapy in our center. Recurrence and overall survival were analyzed for low and intermediate GOG score groups.

Results: The median follow up for both groups (low and intermediate GOG score group) was 45.0 months (range: 10.0-80.8 months). There was no recurrence or death noted in the low GOG score group while two patients (12.5%) recurred in intermediate GOG score group. Three years overall survival were 100%, in the low and 82%, in the intermediate GOG score group of patients.(p=0.065).

Conclusion: Our analysis showed that intermediate GOG scoring group may have better survival and recurrence free survival if subjected to post operative adjuvant treatment. Clinician should weight between survival advantages and potential treatment related toxicities in deciding the best form of adjuvant therapy.
COMPARATIVE STUDY OF VISUAL INSPECTION OF THE CERVIX USING ACETIC ACID (VIA) AND PAPANICOLAOU (PAP) SMEARS FOR CERVICAL CANCER SCREENING

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Background: This study was a comparative study of two screening methods for pre invasive lesions of the cervix. The Papanicolaou (Pap smear), an old and tested screening method was compared with findings of Visual inspection of the cervix following acetic acid wash (VIA). VIA is a new screening method being advocated by the World Health Organization as an alternative to Pap smear in low resource settings.

Objective: To compare the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of VIA and Pap smear.

Methods: This was a comparative study carried out in the postnatal clinic of Ahmadu Bello University Teaching Hospital Zaria. Pap smear samples were taken by the researcher. Samples were fixed in 95% ethyl alcohol for reporting.

The cervix was then painted with 3-5% acetic acid and observed for aceto-white lesions. Suspected areas were biopsied for reporting. Patients with positive Pap smear results were also called back for biopsy. Biopsy served as the reference standard.

Results: There were 351 samples that were suitable for statistical analysis. The sensitivity of VIA was 60%, specificity was 94.4%, Positive predictive value was 50%, and negative predictive value was 99.4%. Accuracy was 98.6%. Pap smear had a sensitivity of 60%, specificity of 100%, positive predictive value of 100%, negative predictive value of 99.4% and accuracy of 99.4%.

Conclusion: VIA had a comparable result with Pap smear. It should be incorporated into our national screening programme to complement cervical cytology in low resource setting like ours.
Poster Session II

NURSE-LED SCREENING PROGRAMME FOR CERVICAL CANCER COMBINES HEALTH PROMOTION AND PSYCHOSOCIAL SUPPORT WITH LOW PERCENTAGE OF TISSUE SAMPLE ERRORS

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Background: In Denmark approximately 300 women are newly diagnosed with cervical cancer each year. In addition a number of 6000 conus are performed. A prophylactic screening programme addressing women aged 23 - 65 years contributes in reducing the incidence and mortality of the disease. However, no more that 60 % of the female population are following the screening programmes.

Aim: In this abstract a nurse-led cervical cancer screening programme is presented in terms of its organisation and content.

Method: The nurse-led cervical cancer screening programme is situated at the outpatient clinic at a Danish University Hospital. Two certified specialist nurses are independently performing kolposcopy and diagnostics in women with cervical dysplasia. They are working together as a team, however supervised by a senior consultant. In this way technical excellence in sampling is combined with health promotion and psychosocial support.

Results: While the time consumption of the consultation remains unchanged, the results show no more than 2.5 percent non-representative tissue samples. In addition the women’s confidence and satisfaction in relation to the gynaecological examination and the tissue biopsies has increased.

Conclusion: The nurse-led cervical cancer screening programme combines health promotion and psychosocial support with a very low percentage of tissue sample errors. The flexible and supportive approach might generate a more stable attendance to cervical screening programmes in future.
Poster Session II

COST OF CERVIX CANCER SCREENING IN A LOW RESOURCE SETTING IN AFRICA

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Introduction: Cancer of the cervix is the second most common cancer-affecting women worldwide and the most common cancer-affecting women in sub Saharan Africa.

It affects younger women than other cancers. Strategies for introducing or strengthening cervical cancer prevention programs must focus on ensuring that appropriate, cost-effective services are available and that women who most need the services will, in fact, use them. It is therefore essential that cervical cancer prevention efforts eliminate the most critical barriers that affect women’s participation, as well as identify and foster conditions that support their use of services.

Methods: Clinic started at central hospital with study of 150 patients and then expanded to 1000 over the next year.

Expansion to outreach clinics was needed to build capacity.

Cost included training of nurses acquiring equipment.

Quality needs to be part of any program and maintaining a database is essential to understanding the outcomes.

Results: From May 2011 to Feb 2012, 6383 women were screened.

Cost of screening 6383 was USD 1809.77

Cost per screen was USD 0.285.

Cost per positive screen was USD 9.382

Cost per treatment of dysplasia to prevent cervix cancer was USD 9.7

Conclusion: Cost of cervix cancer screening is USD 0.285 per client and this is cheap compared to cytology based screening strategy that costs USD 8.08

For the screening program to be sustainable, we propose that clients be encouraged to cost share by paying at least USD 1.
KNOWLEDGE OF CERVICAL CANCER SCREENING AND HPV VACCINATION AMONG A LOW-INCOME POPULATION IN BUENOS AIRES, ARGENTINA

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Objective: To determine the knowledge of cervical cancer screening (CCS) and HPV vaccination among women attending a university-based clinic in Buenos Aires, Argentina.

Methods: A cross-sectional study. An anonymous thirty-seven multiple-choice questionnaire was distributed. A knowledge score was created with the five questions pertaining to CCS. Based on correct answers, a scale from 0 - 5 defined knowledge levels in two categories "good" (score ≥ 3) and "poor" (score ≤ 2). Chi-square or Fisher's exact test were used to compare categorical variables. Unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by simple logistic regression.

Results: 141 subjects were recruited. Sixty-seven percent (n = 95) of all participants were over the age of 30 and 77% (n = 109) were Argentinean. Forty-nine percent (n = 46) attended secondary school, and 33% (n = 46) University. Fifty-eight percent had “good” knowledge scores (n = 77). Seven percent (n = 9) had never had a Pap smear and 69% (n = 97) had a Pap within the last year. Thirty-seven percent (n = 52) never heard about the HPV vaccine and 80% (n = 104) expressed interest in receiving the vaccine. Health insurance was the only statistically significant socio-demographic variable associated with “good” knowledge (OR 2.1, CI 1 - 4.2), and this was strongly associated with knowledge of the HPV vaccine (OR 3.9, CI 1.8 - 9.6) and willingness to vaccinate their children (OR 2.6, CI 1 - 6.5).

Conclusions: Knowledge about CCS and HPV was limited. HPV vaccination acceptance rate was high but none of the surveyed subjects had received the vaccine. Lack of awareness and mechanisms to guarantee access to the HPV vaccine to the low-income sector of the population might explain these results. Future efforts should be focused on educating the population and improving access to the vaccine.
**Poster Session II**

**SURGICAL OUTCOMES OF FERTILITY-SPARING RADICAL ABDOMINAL TRACHELECTOMY**

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The one of the fertility-sparing surgery for the uterine cervical cancer is the radical abdominal trachelectomy. We conducted a study from 2002 to 2010 for the purpose of evaluating surgical outcomes and safety of the radical abdominal trachelectomy.

We registered the patients that strongly desired for fertility-sparing, squamous cell carcinoma, FIGO stage Ia2~Ib1, the tumor diameter were < 2cm, and no involvement of the extra-cervix, no evidence of metastasis (lymph nodes, other organs).

The totals of 21 patients were registered. The median of the age was 32 years old. The median operation times were 330 minutes. The median amounts of bleeding were 1,225g. The median follow-up periods were 36.9 months. A patient showed recurrence of cancer. The patient who relapsed in the pelvic cavity and lung metastases 3 months after surgery was treated with concurrent chemoradiotherapy and chemotherapy. She died on 15 months after surgery. Pregnancy was found in two patients until now. Cesarean delivery was performed at 35 weeks gestation in one case. In the other case artificial abortion was performed at first trimester.

Radical abdominal trachelectomy spent more operation time and tended to more blood loss compared with radical hysterectomy. The recurrence rate was 4.8% (1/21), so that radical abdominal trachelectomy seemed to be a reasonable option for selected patients. A goal of radical abdominal trachelectomy was delivery without the trouble. Because our preliminary results were insufficient, it should be emphasized that further studies are needed, with larger sample sizes and longer follow-up periods.
Poster Session II

RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF ORAL LACTOBACILLI TO FACILITATE THE CLEARANCE OF GENITAL HIGH RISK HPV INFECTION IN WOMEN

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Introduction: Chronic HPV (human papilloma virus) infection was related with incidence of cervical cancer. Patients with vaginal infection were suffered from higher HPV infection rate than those without vaginal infection. Therefore, bacterial vaginosis presented synergy effect on vaginal virus infection. Lactobacilli, the predominant vaginal commensal microbes, was abundant as $10^7$-$10^8$ CFU/g. The absence of vaginal Lactobacilli was the major cause of bacterial vaginosis. Local reduced of Lactobacilli induced 2-4 times vaginitis and recurrence urinary tract infection. At present, the predominance of vaginal Lactobacilli was crucial in the prevention of vaginal infection.

Materials and methods: Women with high risk HPV infection but pap smear without HSIL were enrolled. The women were randomly assigned to the oral lactobacilli group or placebo groups in 1:1 ratio with computer-generated random numbers. Women in both groups received HPV test, pap smear and vaginal gram stain every three months.

Results: Of the 80 women eligible for the study, 60 had three or more visits. 40 were randomised to oral lactobacilli group, and 40 to placebo group. The prevalence of women with HR-HPV DNA detected in 3rd, 6th, and 9th month visits were 67.7%, 55.9%, 52.9% in lactobacilli group, and 73.3%, 70%, 66.7% in placebo group. The median time to HPV clearance was shorter in lactobacilli group. Women in the placebo group had a significant higher percentage of subsequent CIN lesion during follow-up.

Conclusion: Clearance time of HR-HPV infection was shorter in women using oral lactobacilli. Further study investigating the mechanism of lactobacilli in HPV clearance is warranted.
Poster Session II

STUDY OF BIOLOGICAL TUMOR VOLUME AND $SU_{\text{MAX}}$ OF THE PRIMARY TUMOR IN LOCALLY ADVANCED CERVIX CARCINOMA

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Aim: Physical tumor size relates with the clinical outcome of carcinoma cervix. The biological tumor volume of the primary (pBTV) as specified by 18F-FDG avid tumor cells may also serve as a prognostic factor. We intend to find this correlation in our study.

Methods: 15 patients of locally advanced carcinoma cervix had their PET-CT scan done before the radical treatment which consisted of pelvic irradiation with concurrent weekly cisplatin and intracavitary brachytherapy. Maximum Standardized Uptake Value ($SU_{\text{MAX}}$) and pBTV (taken from 40% $SU_{\text{MAX}}$) were calculated from the scans. The disease status was recorded during each routine follow-up subsequently.

Results: Six patients had FIGO stage IIB and nine had stage IIIB disease. The mean pBTV was 52.3 ± 34.2cc (45.4cc in IIB, 57.5cc in IIIB) and the mean $SU_{\text{MAX}}$ of the primary tumor was 8.8 ±4.9 (10.3 in IIB, 7.8 in IIIB). There were no difference in these values between patients with and without disease at six months of treatment (mean pBTV=60.7 vs 49.9cc, p=0.442 and mean $SU_{\text{MAX}}$=11.2 vs 8.2, p=0.649). Also there was no correlation between pBTV and $SU_{\text{MAX}}$ in our patients (Pearsons coefficient=0.09).

Discussion and conclusion: In our study, the pBTV as well as the $SU_{\text{MAX}}$ of the primary tumor did not differentiate patients based neither on FIGO stage nor the treatment outcome. Possible errors in clinical FIGO staging in evaluating the extent of primary tumor might have confounded the correlation. Studies comparing three dimensional physical and biological volume of tumor might help in understanding the impact of pBTV on disease outcome.
Poster Session II

RISK FACTORS OF DIAGNOSTIC DISCREPANCY BETWEEN COLPOSCOPIC-DIRECTED PUNCH BIOPSIES AND LOOP ELECTROSURGICAL EXCISION PROCEDURE (LEEP) CONIZATION OF THE CERVIX

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Objective: The goal of this study was to determine the clinical factors independently associated with diagnostic discrepancy of patients were performed colposcopically directed punch biopsy and leep conization.

Methods: Two hundred and fifty-eight patients (median age 42.2 years; range 15-78 years) referred with a punch biopsy and treated with electrosurgical conization in Daejeon St. Mary's hospital of the Catholic university were evaluated. Three types of deviation of biopsy diagnosis were considered: (1) CIN 2,3,CIS diagnosis, defined as a cone diagnosis of CIN1, atypia and benign reactive changes, and (2) CIN 2,3,CIS diagnosis, defined as a cone diagnosis of microinvasive and invasive squamous carcinoma. (3) CIN 1, atypia, benign reactive changes diagnosis, defined as a cone diagnosis of CIN2,3,CIS, microinvasive and invasive squamous carcinoma. Multinomial logistic regression analysis was used to assess the determinants of the probability of each type of deviation.

Results: Confirmed diagnosis had positive association of punch diagnosis, age, HPV, number of spontaneous delivery, pap smear, and punch specimen number involved. The probability of unconfirmed high-grade CIN diagnosis (n=52, 20.2%) was inversely related to severity of Pap smear and HPV16 positive. The probability of nondiagnosis of carcinoma (n=17, 6.6%) was positively related to severity of Pap smear. The probability of unconfirmed low-grade CIN diagnosis (n=13, 5.0%) was only related to Pap smear.

Conclusions: Our study couldn't confirm previous observations regarding the positive association of patient age and invisibility of squamocolumnar junction with the probability of nondiagnosis of carcinoma. Pap smear and HPV16 positive were shown to be related to the discrepancy of punch and a cone diagnosis.
Poster Session II

PELVIC EXENTERATION FOR RECURRENT CERVICAL CANCER IN PREVIOUSLY IRRADIATED PELVIS


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Objectives: To analyze the morbidity and survival outcomes after pelvic exenteration for central pelvic recurrence after pelvic irradiation in patients with cervical cancer.

Methods: A review was performed on 37 patients who tried pelvic exenteration with curative intent for recurrent cervical cancer in central pelvis after pelvic irradiation.

Results: Pelvic exenteration was completed in 34 patients (92%) and was abandoned in three patients (8%) due to the discovery of peritoneal disease during surgery. The type of exenteration was total in 16 patients (47%), anterior in 11 patients (32%), and posterior in 7 patients (21%). Resection margin negative resection was possible in 32 patients (94%). Thirteen patients (38%) suffered from major postoperative complications and two patients (6%) required reoperation. There was no postoperative mortality. The median follow-up time after pelvic exenteration was 30 months (range, 4-90 months). Fifteen patients (44%) had recurrent disease and 13 patients (38%) died of disease. The 5-year disease-free survival and overall survival was 51% and 52%, respectively. In multivariate analysis, tumor size > 4 cm was the only significant factor which was associated with higher risk of recurrence (Odds ratio [OR], 6.41; 95% confidence interval [CI], 1.29-31.85; P=0.023) and death (OR, 5.29; 95% CI, 1.15-24.32; P=0.032) after pelvic exenteration.

Conclusion: Pelvic exenteration was a potentially curative treatment for selected patients with recurrent cervical cancer in central pelvis after pelvic irradiation although postoperative morbidity was somewhat frequent. Tumor size > 4 cm was an independent risk factor for recurrence and death after pelvic exenteration.
Poster Session II

CLINICAL SIGNIFICANCE OF CHANGES IN PERIPHERAL LYMPHOCYTE COUNT AFTER SURGERY IN EARLY CERVICAL CANCER

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Introduction: The purpose of this study was to investigate the clinical significance of changes in peripheral lymphocyte counts after abdominal type III radical hysterectomy for the treatment of cervical cancer, and to identify clinicopathological factors that are associated with surgery-induced immune disturbances in patients with early cervical carcinoma.

Design: Patients with clinically staged cervical carcinoma (IB to IIA) who were treated at Samsung Medical Center, Seoul, Korea from 1994 to 2007 were retrospectively enrolled. We compared peri-operative peripheral lymphocyte counts, tumor-infiltrating lymphocyte scores, and survival in patients with early cervical cancer treated by abdominal type III radical hysterectomy.

Results: The sample included 756 patients. The median age was 48 years. The median follow-up was 58 months and the five-year survival rate was 93.2%. There was a positive correlation between pre-operative peripheral lymphocyte counts and tumor infiltrating lymphocyte score. Pre-operative peripheral lymphocyte counts decreased significantly after surgery. In multivariate analyses for recurrence, higher pre-operative peripheral lymphocyte counts and recovery of lymphocyte counts (more than 100/µL from the pre-operative level) on post-operative day 3 were independent positive prognostic factors and LN metastasis was negatively associated with post-operative recovery of peripheral lymphocyte counts.
Alterations in peripheral lymphocyte counts after surgery (A), scatter plot of pre-operative peripheral lymphocyte counts and tumor-infiltrating lymphocyte score (B), and peripheral lymphocyte counts on POD 1 (C) and POD 3 (D)

[1]
A: Disease-free survival

- Before surgery
  - Higher lymphocyte count (> 50 percentile)
  - Lower lymphocyte count (≤ 50 percentile)

  $P = 0.122$

- POD3
  - Higher lymphocyte count (> 50 percentile)
  - Lower lymphocyte count (≤ 50 percentile)

  $P = 0.308$

- POD3
  - Increase of lymphocyte count from pre-operative level
  - Equal or decrease of lymphocyte count from pre-operative level

  $P = 0.085$

- POD3
  - Increase of lymphocyte count more than 100 μL from pre-operative level
  - Decrease, equal, or increase of lymphocyte count less than 100 μL from pre-operative level

  $P = 0.136$
Conclusion: Peripheral lymphocyte counts after cervical cancer surgery are important prognostic factors, and management aimed at minimizing immune disturbances after surgery should be assessed, especially in patients with LN metastasis.
Poster Session II

PATTERNS OF RECURRENCES AND PROGNOSIS IN SQUAMOUS CELL CARCINOMA OF UTERINE CERVIX: A 10-YEAR EXPERIENCE OF SINGLE INSTITUTION

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Objective: To assess the pattern of failure and to analyze the variables predictive of the risk of local, distant and retroperitoneal disease recurrence.

Material and methods: Of a total of 1,280 uterine cervical cancer patients, medical records of 201 recurrent cases were retrospectively reviewed. The associations of the sites of recurrence with risk factors for recurrence and survival rates were analyzed.

Results: Mean follow-up period was 54 months (range 0-364 months). Overall recurrence rate was 15.7% (201/1280). Five-year overall survival rate of recurrent cases was 84.5%. Local organ invasion, intra-abdominal and extra-abdominal distant metastasis, and retroperitoneal recurrence were 49.7%, 9.1%, 44.7%, and 42.1%, respectively. Parametrial involvement was significantly associated with local organ invasion ($P = 0.043$) and extra-abdominal distant metastasis ($P = 0.017$). Local organ invasion ($P < 0.001$) and extra-abdominal distant metastasis ($P = 0.003$) were significantly associated with lymph node (LN) metastasis. Invasion of more than two thirds of cervical stroma was also increased in local organ invasion ($P = 0.006$) and extra-abdominal distant metastasis ($P = 0.048$). Multiple regression analysis revealed that intra-abdominal distant metastasis was the most independent risk factor for disease-related mortality (hazard ratio 3.888; 95% confidence interval 1.092-13.836; $P = 0.036$).

Conclusion: Parametrial involvement, LN metastasis, and deep stromal invasion seem to be risk factors for local organ invasion and extra-abdominal distant metastasis in uterine cervical cancer. Intra-abdominal distant metastasis might be the rarest, but, most lethal recurrence sites in cervical cancer patients.

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Poster Session II

FEASIBILITY OF DOSE ESCALATION USING A MULTICHANNEL VAGINAL APPLICATOR WITH INTRAUTERINE BRACHYTHERAPY FOR CERVIX CANCER WITH EXTENSIVE VAGINAL INVOLVEMENT

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Background: In cervical cancer, it may be necessary to replace the standard brachytherapy tube/tandem with a single channel intrauterine tube with cylindrical vaginal applicator to encompass vaginal disease. Tumour coverage is often compromised due to high normal tissue doses and by limited optimisation options. A new vaginal applicator with multiple surface channels and a central channel (Nucletron) enables asymmetrical dose distributions to boost selected vaginal sections. We aimed to examine whether dose escalation was feasible using a multichannel versus single channel applicator.

Methods: Five patients with vaginal involvement had HR-CTV and OAR delineated on a CT scan acquired with single channel tube (IUT) in situ. Library software was used to reconstruct the corresponding multichannel vaginal applicator (MCV). Plans were optimised aiming to improve CTV coverage while at least maintaining OAR doses. Prescribed dose was then increased to GEC-ESTRO OAR limits: EQD2 D2cc rectum 75Gy, sigmoid 75Gy, bladder 95Gy.

Results: HR-CTV coverage was improved for all patients with mean IUT D90 85% (range 70-101) versus 96% (73-135) with MCV. Prescription dose was increased by 0.5-1.5Gy and total HR-CTV D90 increased from mean 64Gy (range 60.4-66.4Gy) to 67.6Gy (64.2-69.7) (p=0.03). Rectal tolerance limited dose in 4 patients (73.8-74.4Gy) and sigmoid in one (73.7Gy). Further escalation may be feasible if MRI rather than CT was used for HR-CTV definition.

Conclusions: Multichannel optimisation improved HR-CTV coverage and reduced OAR doses. This study demonstrates the feasibility of escalating tumour dose (mean 3.6Gy (2.0-8.0)) using a multichannel versus single channel applicator for significant vaginal disease.
Poster Session II

STEREOTACTIC BODY RADIOTHERAPY IN CASES UNSUITABLE FOR GYNECOLOGICAL BRACHYTHERAPY

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Purpose: To present early results of Stereotactic Body Radiotherapy (SBRT) for patients unsuitable for standard intracavitary gynecological brachytherapy.

Methods: A prospective data base of cases that are unfavorable for standard gynecological brachytherapy and are treated with SBRT boost is maintained at our centre. Six gynecological cancer patients were deemed in-operable due to severe co-morbidities/advanced disease were treated with radical radiation therapy. All patients received standard whole pelvis 4500 cGy / 25 #'s external beam radiotherapy followed by SBRT boost, dose: 1500-2000cGy / 3-4 fractions in place of brachytherapy. A vaginal cylinder was inserted at the time of CT simulation for target localization. Daily cone beam match was done prior to each SBRT fraction.

Results: Patients age:range 55-83yrs were treated with SBRT. PTV coverage range: 86-100%; Rectal doses range:1067-2040cGy; Bladder doses range: 1250-2468cGy. Acute RTOG GI Grade 2 and GU Grade 1 toxicity was noted in all patients. Followup range:2-12months, all patients are alive with clinically loco-regionally controlled disease. Patients tolerated the treatment well with no treatment breaks or serious adverse reactions.

Conclusion: In our early experience SBRT boost appears to be a reasonable option for cases that are not suitable for standard gynecological brachytherapy. Further follow-up is necessary to define its role in gynecological cases.

[SBRT plan]
Poster Session II

THE ROLE OF ATM AND TGFβ1 GENE POLYMORPHISMS IN LATE TOXICITY PREDICTION IN PATIENTS TREATED WITH CHEMORADIOTHERAPY FOR CERVICAL CARCINOMA

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Background and aims: The Goal of study was to find out, whether there is statistically significant association between late toxicity occurrence in patients treated with radiotherapy for locally advanced cervical carcinoma and occurrence of the ATM (ataxia telangiectasia mutated), TGFβ1 (transforming growth factor β1) SNPs (single nucleotide polymorphisms).

Methods: 55 patients examined with 102 healthy controls. Patients treated with chemoradiotherapy in years 2001-2010. Dose on pelvis 46-60Gy, parametria 9-14Gy (in 50 patients), paraaortal nodes 44Gy (in 28 patients), brachytherapy doses 18-30Gy. Chemotherapy - cisplatin 40mg/m2/weekly in 52 patients, in 3 patients paclitaxel 45mg/m2/weekly, in 8 patients both drugs were used. Late toxicity was assessed according to RTOG/ EORTC criteria.

DNA extracted from peripheral lymphocytes. SNPs analyses: ATM gene polymorphism (5557G>A) and TGFβ1 gene polymorphic loci -800 G>A, -509 C>T - with restriction fragment length analysis, TGFβ1 gen deletion -1552 with fragment analysis and TGFβ1 gene codon L10P with direct sequencing of PCR product.

Logistic regression used for analysis of relationship between patients characteristics or genetic markers and grade of complications. For multiple comparison Bonferroni correction used in selected predictors after univariate analysis with p< 0.05.

Results: Statistically significant predictor of late toxicity grade III-IV after Bonferroni correction is SNPs combination of TGFβ1 gene - TRIPLE (509C>T, L10P, del 1552 AGG) and DOUBLE1 (509C>T, L10P) homozygot genotypes (p< 0.021). From therapeutic factors it is dose 14 Gy used on parametria (p< 0.006).

Conclusion: We proved statistically significant association between genetic markers- TRIPLE/ DOUBLE1 homozygot genotypes and late toxicity grade III-IV.
Poster Session II

LAPAROSCOPIC LYMPH NODE DISSECTION SHOULD BE PERFORMED BEFORE FERTILITY PRESERVING TREATMENT OF PATIENTS WITH CERVICAL CANCER

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Aim: To assess our results of treatment of women with stage I cervical cancer > 2cm seeking fertility preservation. Treatment consisted of Laparoscopic Pelvic and Paraaortic Lymphadenectomy (LPPLND), and when no nodal metastasis was detected, neoadjuvant chemotherapy (NACT) followed by radical vaginal trachelectomy (RVT). Patients with positive lymph nodes underwent primary chemoradiation.

Methods: A cohort of women younger than 40 years of age with stage I disease > 2 cm who underwent LPPLND and either NACT and RVT or chemoradiation. Oncological outcome was evaluated.

Results: Eighteen women were eligible for this study. Twelve (67%) women were diagnosed with metastasis in > 1 pelvic and/or paraaortic lymph nodes, and thus received primary chemoradiation. After a mean follow-up of 25.5 months, three out of these 12 women (25%) developed recurrence. Six women (33%) underwent NACT and RVT. Three patients experienced complete response to NACT and three patients showed more than 50% tumor size reduction. After a mean follow-up of 30.6 months all six women are free of recurrence. One patient delivered a healthy infant.

Conclusions: Staging LPPLND allows separating patients in high or low recurrence risk groups. NACT and RVT seems to be safe for women with completely staged stage I cervical cancer > 2 cm in diameter, whereas even after primary chemoradiation, patients with positive lymph nodes experienced recurrence. Therefore, selection of patients with stage I cervical carcinoma > 2 cm, eligible for fertility preservation should include histopathologic evaluation of lymph node status before further treatment.
Poster Session II

EVALUATION OF RETROPERITONEAL PARAORTIC LYMPHADENECTOMY IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER

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Objective: To evaluate the indication of retroperitoneal paraaortic lymphadenectomy in patients with locally advanced cervical cancer, with or without abnormal pelvic or common iliac nodes on imaging.

Methods: This retrospective descriptive study included all patients undergoing a retroperitoneal paraaortic lymphadenectomy for locally advanced cervical cancer between January 2005 and December 2011. Descriptive statistics, Kaplan Meier analysis, Fisher exact test and Chi-square test were used.

Results: Fifty-seven patients were included. All had at least a stage 1B2 tumor and squamous carcinoma was present in 79% of cases. Mean age at diagnosis was 48.3 years (29-77). An average of 12 paraaortic nodes were removed (2-33) and 12% of patients had confirmed metastatic nodes on histopathologic analysis. Intra-operative complication rate was 5%. Post-operative complications included 4 simple and 3 infected lymphoceles. Every patient had preoperative imaging (CT-scan 79%; TEP-CT 18%; MRI 60%). Abnormal pelvic (p=0.002) or common iliac nodes imaging (p=0.001) were statistically associated with metastatic paraaortic disease on histopathologic analysis. No metastatic paraaortic node was identified when both pelvic and common iliac imaging were normal. Mean follow up was 33 months (1-69) and 5-year progression free survival was 79%.

Conclusion: Abnormal pelvic or common iliac nodes on imaging are strongly associated with metastatic involvement of the paraaortic nodes. In the presence of normal pelvic and common iliac imaging, our data suggests that there is no indication to the retroperitoneal paraaortic staging in patients with locally advanced cervical cancer.
Poster Session II

10 YEARS EXPERIENCES WITH LESS RADICAL SURGERY FOR STAGE I CERVICAL CANCER PATIENTS

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Background and aims: The purpose of the study was to determine feasibility and oncological safety of less radical surgery for cervical cancer patients. There was LAP II protocol established: laparoscopic lymphadenectomy with sentinel lymph node identification (SLNI) followed by vaginal hysterectomy type A.

Methods: Patients with invasive cervical cancer FIGO stage IA1 angioinvasion+, IA2 and IB1 (less than 2 cm, less than ½ stroma) were indicated for less radical procedure: laparoscopic SLNI (patent blue+Tc99), frozen section. In case of positive frozen section conversion to Wertheim C2. If SLN were negative procedure was followed by extirpation of lymphatic channel from parametrium - “selective” parametrectomy, systematic pelvic lymphadenectomy and vaginal hysterectomy.

Results: In 2002-2011 were 114 women suitable for criteria operated. 11x IA1 (9.7%) angioinvasion+, 19x IA2 (16.3%) angioinvasion+ 6x (32%), 84x IB1 angioinvasion+ 27x (32%). Follow-up 126-6 month. Totally 7 patients 6.1% had metastasis in sentinel lymph-node. 4x detected by frozen section and converted to Wertheim. 3x detected by definitive histopathology+immunohistochemistry with adjuvant radiation. In last two years SLNI detection rate was 100%, side specific detection rate 100%. Detection and extirpation of lymphatic channel were performed in all patients. Detection rate 100%, side specific detection rate 86%. No recurrence in follow-up was detected.

Conclusions: Highly selected cervical cancer patients group with primary excellent prognosis had 6.1% metastasis presence in sentinel lymph node. LAP II less radical conservative protocol for sentinel negative patients has in our series excellent oncology results compared to standard radical procedure. Detection of lymphatic channels in parametrium/selective parametrectomy is feasible with high detection rate.
Poster Session II

IN VITRO CHEMORESPONSE ANALYSIS AND CLINICAL OUTCOMES IN CERVICAL CANCER

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Background and aims: The objective of this study was to report clinical outcomes of cervical cancer patients treated with weekly cisplatin chemo radiation therapy (chemoRT) based on pre-treatment cisplatin chemoresponse testing.

Methods: This was a retrospective analysis of patients with cervical cancer seen at our institution between May 2009 and August 2011. Patients were treated with concurrent weekly cisplatin chemoRT and underwent pre-treatment in vitro chemoresponse testing (Precision Therapeutics, Inc.). The study consisted of 33 patients with FIGO stages Ib2 to IIb disease. Pre-treatment chemoresponses were determined from chemoresponse dose response curves and were scored as responsive (R), intermediate (IR), or nonresponsive (NR).

Results: There were 28 patients with squamous cell carcinoma and 5 with adenocarcinoma. cisplatin chemosensitivity was R and IR in 18 patients and NR in 15 patients. The 2-year recurrence-free survivals (RFS) were 87% for the patients who tested R + IR to cisplatin compared to 58% for those who were NR to Cisplatin (p = 0.047). For patients with squamous cell histology, the 2-year RFS were 86% for the R + IR group compared to 46% for those NR to cisplatin (p = 0.01). Stepwise proportional hazards modeling of RFS demonstrated chemoresponsiveness to cisplatin (p = 0.029) and FDG-PET lymph node status (p = 0.011) were the only independent predictors of RFS for patients with squamous cell histology.

Conclusion: Pretreatment in vitro cisplatin chemoresponse analysis of cervix cancer biospecimens was technically feasible and predictive of RFS outcome in patients treated with weekly cisplatin chemoRT.
Poster Session II

P16 EVALUATION AS A PROGNOSTIC FACTOR OF CERVICAL DYSPLASIA

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Introduction: Protein p16 as an important cell-cycle inhibitor is a promising diagnostic and prognostic factor of cervical dysplasia. In our study we evaluate the impact of p16 protein evaluation on management of cervical dysplasia.

Patients and methods: A retrospective study was performed on 122 consecutive patients with colposcopically-directed cervical biopsy (CDB) with following excisional procedure (LEEP or cold-knife conisation). P16 expression in the specimen from CDB was independently evaluated by immunohistochemistry in all patients. Relation among CDB histology, p16 expression and final histology from excisional procedure was analysed.

Results: In our series, we identified 44 CIN I and 61 CIN II/CIN III in CDB specimens. In the CIN I group, 15 cases (34,1%) were p16 negative and 29 (65,9%) cases were p16 positive. In CIN I p16 negative group, only 2 of 15 patients (13,3%) had CIN II/CIN III in the final histology comparing to 19 of 29 patients (65,5%) in CIN I p16 positive group (statistically significant, p< 0,05; Wilcoxon test). In CIN II/CIN III group, 60 (98,4%) specimen were p16 positive and 57 patients (93,4%) had also CIN II/CIN III in the final histology.

Conclusion: In our study of 122 patients with CDB we found that in group of CIN I patients, p16 evaluation had significant predictive value for final histology. In the group of patients with CIN II/CIN III, 98% specimens were p16 positive and therefore p16 evaluation had no prognostic impact on final histology. Prospective study is needed to confirm this data.
POSTER SESSION II

NEUROENDOCRINE CARCINOMA OF THE CERVIX: A SINGLE INSTITUTION’S EXPERIENCE

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BACKGROUND: Neuroendocrine carcinomas (NEC) of the cervix comprise only 2% of all cervical cancers. Prospective data is limited and treatment guidelines rely on literature from lung NEC. The objective of this study was to report on our experience in the management of this rare disease.

METHODS: This was an IRB-approved, single-institution, retrospective review. Study criteria included patients with cervical NEC diagnosed between 1990-2011. Demographic, treatment and survival data was collected and progression free survival (PFS) and overall survival (OS) were assessed.

RESULTS: A total of 24 patients met inclusion criteria. The median age at diagnosis was 43. Advanced-stage disease (Stage II-IV) was diagnosed in 61% (n=15) of patients. Of the 9 patients with stage I disease, 4 were treated with platinum-based neoadjuvant chemotherapy, 5 were treated with initial radical surgery, and 7 had adjuvant therapy. Mean PFS and OS was 36 and 55 months, respectively. Two of 15 advanced-stage patients were treated with surgery, adjuvant chemotherapy and radiation while the remaining were treated with a combination of chemotherapy and/or radiation. Advanced-stage patients had a mean PFS and OS of 18 and 20 months, respectively. At last follow-up, 78% of stage I versus 13% of advanced-stage patients were alive.

CONCLUSION: We report one of the largest single-institution experiences of neuroendocrine cervical cancer. Advanced-stage patients had a poor prognosis regardless of therapy. However, multi-modality therapy in early-stage disease portended an excellent prognosis, supporting the goal of curative intent.
Poster Session II

HORMON REPLACEMENT THERAPY AFTER CURATIVE THERAPY OF CERVICAL CANCER

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There are concerns that contact with hormone replacement therapy drugs (HRT) of cancer patients with postovariectomy syndrome (POES) can initiate the growth of neoplastic tumors. The main target of investigation is to evaluate POES manifestations and to motivate the possibility of HRT assigning to patients with POES after curative therapy of cervical cancer (CC) at differentiated approach.

There are summarized results of clinical observations over 156 patients after curative therapy of CC at Ia - IIa stages in Udmurt Oncologic Dispensary within the years 1995-2004. The investigation includes 60 patients of childbearing age and 96 patients of premenopausal period. The manifestation rate of neurovegetative, psychoemotional, metabolic endocrine syndromes under modified menopausal Kuperman index and urogenital atrophy under Bachman J.A., 1994 were evaluated. 78 pairs of patients “accepting HRT control” were selected in this cohort. The treatment was provided by using the combination of estradiol valerate (EV, 2 mg/day during 21 days) with acetate cyproterone (AC, 1 mg/day during the last 10 days of treatment cycle) within 36 months.

The manifestations and formation frequency of POES are presented. Patient selection criteria, indications and contraindications for HRT are formulated. The combination of EV+AC resulted to reduction (p< 0,01) of POES complaints. The patients were observed during 60 months after hormone replacement therapy. CC relapse is not detected. After CC curative therapy at differentiated approach HRT is pathogenically relevant and safe method of POES adjustment.
Poster Session II

OUTCOMES OF CHEMORADIOThERAPy IN CERVICAL CANCer. A FIVE YEARS FOLLOW UP

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Cervical cancer is the second most frequent cancer in women in our country. Since year 2000 we began the use of chemoradiotherapy as the standard treatment for locally advanced cervical carcinoma.

Objectives: To evaluate the efficacy, toxicity and overall survival of chemoradiotherapy in patients with locally advanced cervical carcinoma and to compare with international data.

Methods and materials: Retrospective study of patients with consecutive FIGO stage II B - IV A cervical cancer treated by chemoradiotherapy between 2001 - 2006. Treatment consisted of external-beam radiotherapy with concurrent weekly cisplatin (40 mg/m²), followed by high-dose-rate brachytherapy. The Kaplan-Meier method was used to determine overall survival.

Results: The analysis included 145 women. The median duration of follow up was 60 month (range 4 -120). Overall survival was 53.2%. The median age was 56 years (range 24-93). Histological diagnosis: squamous cell carcinoma 125 (86%), adenocarcinoma 12 (8 %) and undifferentiated carcinoma 8 (6%) patients. Figo stage cervical cancer was II B = 57, III A = 3, III B = 73 and IV A = 8 patients. Local recurrence was documented in19 patients and 14 with distant metastases, 25 patients had severe (grade 4) adverse effects.

Conclusions: The overall survival outcomes in this group of women with locally advanced cervical carcinomas treated with chemoradiotherapy is unfavourable comparing with worldwide data. We believe that the difference is because most of our patients are diagnosed at advanced stage with massive tumoral volume and nodal involvement.
Poster Session II

OUTCOMES AND PROGNOSIS OF PATIENTS WITH RECURRENT CERVICAL CANCER AFTER RADICAL HYSTERECTOMY

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Objective: Our aim is to investigate the clinical features and outcomes following recurrence after primary radical hysterectomy for cervical cancer.

Methods: Clinical data of 121 documented recurrent cervical cancer patients who received primary radical hysterectomy and bilateral pelvic lymphadenectomy between 1993 and 2000 at Chang Gung Memorial Hospital were retrospectively reviewed. Clinicopathological variables, primary treatment, failure pattern, salvage treatment and outcomes were analyzed.

Results: Cancer recurrence was documented at a median time to recurrence (TTR) of 28.4 months (1.2 - 129.9 months). Assessable failure patterns (n = 106) included loco-regional in 35.5%, distant in 32.5% and combined local-distant in 20%. HPV 16-negative, 18-positive, HPV52-positive and recurrence at both pelvic and distant were associated with significantly shorter TTR. 5-year survival of the 121 patients was 22.3% after cancer recurrence. The median survival after recurrence was 16.4 months (range 0-135.3 months). By multivariate analysis, the significant prognostic factors for survival after recurrence were non-squamous histology (HR 1.73, 0.96-3.09; p = 0.06), and extravaginal site of recurrence (HR 2.88, 1.41-5.84; p = 0.003).

Conclusion: Non-squamous histology and extravaginal site of recurrence were significant predictors of death after relapse in recurrent cervical cancer patients who had radical hysterectomy as primary treatment.
**Poster Session II**

**PREOPERATIVE CHEMO-BRACHYTHERAPY FOR LOCAL ADVANCED CERVICAL CANCER**

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**Objectives:** To study the effect of surgery following platinum-based chemotherapy combined radiation therapy and concurrent chemoradiotherapy in treating cervical cancer of stage IB2-IIA.

**Materials:** 101 cases cervical cancer of stage IB2-IIA which were all treated in our hospital during Jan.2003 and Jul.2010 were taken in the study. 59 patients in studying group, who were underwent surgery following chemotherapy one cycle and brachytherapy(2100cGy-2400cGy). 42 cases treated by concurrent chemoradiotherapy in control group.

**Methods:** Short term therapeutic effect, adverse reaction and survival time between two groups were compared.

**Results:** After chemotherapy combined brachytherapy 100% cases can be operated radically and 93.2% can reach pathological response in study group. There was no difference between these two groups in the effective rate after treatment. The 5 years- progression-free survival(PFS) rates were 84.3% and 92.8%,and 5 years-overall survival(OS) rates are 87.7% and 93.8% in study and control groups respectively by Kaplan-Meier. There was no difference in PFS and OS between two groups by log-rank test.

**Conclusions:** The effect of surgery following chemotherapy combined brachytherapy is same as concurrent chemoradiotherapy in efficiency, while with less chance of adverse reaction.
POSTER SESSION II

ROLE OF VIA AND VILI AS A CERVICAL CANCER SCREENING TOOL IN LOW RESOURCE SETTING

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Introduction and aim: In view of the failure of cytology screening programme for cancer cervix in developing countries, WHO suggested unaided visual inspection of cervix after application of acetic acid (VIA) and Lugol's Iodine (VILI) as alternative screening methods. The present study was done to evaluate VIA and VILI in comparison to pap smear as screening methods for carcinoma cervix in a low resource setting.

Methodology: 328 women were subjected to Pap smear, VIA, VILI and colposcopy.

Results: Sensitivity of Pap smear, VIA and VILI was 20.83%, 55.5% and 86.84% respectively and specificity was 98.38%, 71.39% and 48.93% respectively.

Conclusion: Even though VIA and VILI are less specific in comparison to Pap smear, they are more sensitive in detecting preinvasive lesions. Hence VIA and VILI can be used as cervical cancer screening tool in low resource setting.
Poster Session II

QUALITY OF LIFE AFTER NERVE-SPARING RADICAL HYSTERECTOMY

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Radical hysterectomy (RH) is associated with late morbidity because of damage of pelvic autonomic nerves. The most frequent complication is bladder dysfunction and there are also data about sexual and anorectal dysfunctions. Nerve-sparing technique of radical hysterectomy (NSRH) has been developed in order to reduce surgical treatment related morbidity.

Although the NSRH technique has not become fully standardized, preparation and preservation of superior and inferior hypogastric plexus, hypogastric nerves and pelvic splanchnic nerves is the main principle of this surgical method.

Objective: The aim of this study was to evaluate potential difference in postoperative morbidity in patients treated with nerve-sparing techniques and traditional radical hysterectomy for cervical carcinoma.

Method: In this study, using specifically designed questionnaire, we evaluate three main areas of postoperative morbidity: bladder, sexual and anorectal dysfunction. Patients treated with postoperative radiotherapy were excluded from this study.

Results: 84 patients with NSRH (type C1) and 58 with RH (type C2) were analyzed 5 months after surgery. Bladder dysfunction occurred in 2.5% of patients with NSRH and 25.9% of patients with RH. Anorectal dysfunction was present in 5.9% of patients with NSRH and in 22.4% of patients with RH. There were no significant differences in occurrences of sexual dysfunction in these two groups of patients.

Conclusions: Results of our study implicated that incidence of complications resulted from disturbances of autonomic pelvic nerves were significantly lower in patients with NSRH in comparison with traditional RH. NSRH technique deserves consideration because of improving quality of life in cervical cancer patients.
Poster Session II

SELF-REPORTED BARRIERS AND FACILITATORS TO PREVENTIVE HPV VACCINATION AMONG ADOLESCENT GIRLS AND YOUNG WOMEN: A SYSTEMATIC REVIEW

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Aim: Ontario provides population-based preventive HPV vaccination to adolescent girls yet in the program’s first 2 years only approximately half of eligible girls received it. Improved vaccination uptake is needed to maximize the potential for primary prevention of HPV disease and cervical cancer. We systematically reviewed the evidence concerning barriers and facilitators to vaccination from the viewpoint of adolescent girls and young women.

Methods: We conducted electronic database searches and included studies of self-reports of barriers and facilitators to preventive HPV vaccination among females aged 9-26 years in Canada and the USA. Study quality was appraised. Results were synthesized qualitatively for 9-26 year old females and for 9-17 year old adolescent girls.

Results: Twenty-two studies were included representing the views of 8079 mostly unvaccinated adolescent girls and young women. Twenty-one studies were conducted in the USA and 1 was conducted in Canada; most were quantitative. Twenty-one barriers and 11 facilitators were identified. Cost, feelings of not needing vaccination, and concerns about safety and side effects were the most common barriers. Perceived benefit and health care provider recommendation were the most common facilitators to vaccination. Three studies examined adolescent views separately: not being sexually active and not believing themselves at risk were the most common barriers while parental or health care provider endorsement were the most common facilitators. Study quality was limited by methodological weaknesses.

Conclusions: Tailored health promotion interventions are recommended. There is a need for

1) additional Canadian studies

2) more qualitative inquiry and

3) more studies among adolescents.
ONE-STOP ‘SELECT AND TREAT’ COLPOSCOPY: AN IMPROVED SERVICE FOR LOW GRADE CYTOLOGY REFERRALS?

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Background: Most women with low grade (borderline and mild dyskaryosis) cytology referred to colposcopy undergo punch biopsies under a 'select and treat' strategy. This allows histological confirmation of disease thereby minimising overtreatment. The one-stop clinic employs an Ultra Rapid Microwave Histoprocessor which enables histological diagnosis within two hours and the option of immediate loop biopsy, thereby reducing anxiety and defaulting from treatment.

Objective: To determine the sustainability and patient choice for treatment at the one-stop clinic; and establish the concordance of punch biopsy and loop histology for high grade (HG) cervical intraepithelial neoplasia (CIN).

Methods: Observational study of women with low grade cytology referred to the one-stop colposcopy clinic, Northern Gynaecological Oncology Centre, Gateshead between 2001 until 2011.

Results: Concordance of punch biopsy for CIN 2 or more severe (high grade CIN) with loop histology was >70% for 2090 low grade referrals. Of the 360 women (17%) with HG CIN on punch biopsy, 259 (72%) opted to have immediate loop treatment at the first visit. One hundred and ninety (73%) of these women had HG CIN on loop histology. Of 97 women (27%) who had deferred loop biopsy at a median of 28 days (range 7-112 days), 65 (67%) had HG CIN on loop histology. Attendance at return for treatment appointments was 100% amongst all patients.

Conclusions: This one-stop 'select and treat' colposcopy clinic reduces defaulting from treatment. It has proven to be a sustainable service and patients, when given the choice, prefer to have loop treatment at their first visit.
Poster Session II

STANDARDISATION OF CERVICAL LOOP PROCESSING: IT’S ROLE IN THE CONSERVATIVE MANAGEMENT OF SMALL VOLUME CERVICAL CANCER

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Background: Recently, a trend towards managing small volume cervical cancers with conservative surgery has emerged with encouraging results for recurrence-free survival and fertility preservation. In order to correctly select cases which may benefit from conservative management, such as loop excision and simple hysterectomy, it is becoming increasingly important for pathologists to accurately report tumour dimensions in order to calculate tumour volume.

Objective: To prove the need for standardisation of cervical loop processing to facilitate better estimation of tumour volume, allowing a more conservative approach towards small volume cervical cancer.

Design: Questionnaire survey of loop processing techniques, 23 Pathology laboratories, England 2009-2010

Outcome measures:

1) Indications for cutting levels,

2) Number of levels cut,

3) Technique of handling loop specimens.

Results: In 22 out of 23 laboratories cervical loop specimens were handled by medical staff, using parallel slices. The practice of cutting levels routinely for hand-sliced loop specimens varied greatly amongst laboratories. Twelve of them did not cut levels, 10 cut some and of these 5 did so on all slices. Routine levels were mostly performed for end blocks and uncovered blocks. Eleven out of 23 laboratories cut 3 levels on each slice, and one laboratory cut 6 levels. All laboratories would refer cancer diagnoses to a local MDT but only 18 would refer histology for central review.

Conclusion: Large variation in processing of cervical loop specimens exists. A standardised approach to processing these loops is advised in order to better select cases for conservative management of small volume cervical cancers.
Poster Session II

LINE-1 METHYLATION IN CERVICAL HIGH GRADE LESION

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Objectives: To study LINE-1 methylation of pre-cancerous cervical high grade lesions.

Methods: Eighteen cases of grade 3 cervical intraepithelial neoplasia (CIN 3), 18 cases of normal cervical squamous epithelium (NCSE), 17 cases of cervical adenocarcinoma in situ (AIS) and 20 cases of normal endocervical gland (GL) were recruited. Basic clinical characteristics were collected and the pathological slides were reviewed, then microdissection was performed for DNA extraction. Methylation levels of long interspersed nuclear elements (LINE-1) were measured with a combined bisulfite restriction analysis (COBRA) polymerase chain reaction (PCR) as: complete methylated CpGs (⁵³⁷⁷⁷), two patterns of partial methylated CpGs (⁵³⁷⁷⁷ and ⁷³⁷⁷⁷), and unmethylated CpGs (⁵³⁷⁷⁷).

Results: There were no differences in baseline characteristics between case and control (CIN 3 vs. NCSE and AIS vs. GL). The global methylation and ⁵³⁷⁷⁷ levels were not different between high grade lesions and their normal counterpart. Both cell types of cervical high grade lesions had higher level of ⁵³⁷⁷⁷ than normal tissues (CIN 3: NCSE = 32.98%;27.83%, P = 0.001, AIS: GL = 33.55%;28.19%, P=0.001). However, the high grade lesions had lower level of partial methylated CpGs than in normal tissue (CIN 3: NCSE = 41.53%;50.43%, P = 0.005 and AIS: GL = 38.06%;45.59%, P < 0.001). The methylation levels of all patterns of CIN 3 were similar to those in the AIS group.

Conclusions: Precancerous cervical high grade lesion had higher unmethylated and lower partial methylated LINE-1 than normal tissues. There was no significant difference in methylation level between CIN 3 and AIS.
Poster Session II

THE TREATMENT OUTCOMES OF CERVICAL ADENOCARCINOMA COMPARED TO SQUAMOUS CELL CARCINOMA

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Objective: To compare the survival outcomes of cervical adenocarcinoma (AC) and squamous cell carcinoma (SCC).

Material and method: A retrospective study was conducted to compare the overall survival, disease-free survival and recurrence rates of AC with those of SCC. Survival was analyzed according to the Kaplan-Meier method.

Results: Women with FIGO stages I-IV cervical AC were compared with those with SCC treated in the same period. 508 patients (169 AC, 339 SCC) were analyzed. There were no differences in age, obstetrics history, oral contraceptive use, previous Pap smear, underlying disease, staging and complications from treatment. However, there were differences in symptoms, onset of disease and result of treatment. There were no statistically significant differences in recurrence rate or disease-free survival. However, AC patients had lower overall survival (AC 63.3%: SCC 70.2%, p = 0.048), especially in the advanced stage.

Conclusion: Cervical AC showed the same recurrence and disease-free survival rate, but lower overall survival than SCC, especially in the advanced stage.
Poster Session II

ROBOTIC RADICAL HYSTERECTOMY FOR CERVICAL CANCER- AN INITIAL EXPERIENCE

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Objectives: Robotic surgery offers a new & convincing approach to patient with cervical cancer. The present study was conducted to evaluate the feasibility & outcome of robotic radical hysterectomy with bilateral pelvic lymphadenectomy using da vinci surgical system.

Method: This was a retrospective study which was performed at our institute from March-2011 to March-2012. We studied the patients in term of length of surgery, docking time, Estimated Blood loss, operative complications, yield of Pelvic lymph nodes, vaginal cuff & hospital stay.

Results: 18 of the 21 patient were Stage I. Three of them were post NACT. The median age was 55. The Mean body weight was 63.2kgs. There were no conversions to laparotomy. The mean operative time was 256 min. Docking time on an average was 30 min. The mean blood loss was 120 ml. The average number of pelvic lymph nodes resected was 26.2(13-41). One of them developed perforative peritonitis and subsequently ureteric fistula and one developed bladder injury.

Conclusions: Robotic radical hysterectomy is feasible and associated with minimal morbidity. Even though Short term result are promising, long term oncologic outcome is to yet to be evaluated.
Poster Session II

ATTENDANCE TO MASS SCREENING PROGRAM AMONG YOUNG WOMEN WITH CERVICAL CARCINOMA IN FINLAND

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Background: In Finland 30-60 year old women have been invited to cervical cancer screening with Pap-smear 5-yearly since 1960’s. While the incidence of cervical cancer is low (3.5/100 000), among young women it has increased from 3.0 to 8.2/100 000 women during the last 20 years.

Aim of the study: Compare the frequency of invitations and attendance to screening in cervical cancer patients and their matched controls.

Materials and methods: The study consisted of 99 cervical cancer patients diagnosed at age ≤45 years in 1988 - 2009 at Turku University Hospital and 594 age- and home community-matched controls. Data on the invitation and attendance was collected from the Finnish Mass Screening Registry.

Results: Cervical cancer was diagnosed in 13% age < 30 years, 27% at 30-34 years, 22% at 35-39 years, and 37% at ≥40 years.

22 patients (22%) and 120 (20%) controls were invited to screening during the year of cancer diagnosis. 4 patients (18%) and 7 controls (6%) had previous cytological abnormality. 64% of cancer patients and 73% of controls attended screening.

1-5 years before diagnosis, 70 (71%) of the cases and 457 (77%) of controls were invited to screening and the attendance rates were 49% and 67%. 6-10 years before diagnosis, 49% of patients and controls were invited for screening and 29% and 53% attended.

Conclusion: Attendance to cervical mass screening with conventional Pap smear up to 10 years before cervical cancer diagnosis was significantly lower among women with cervical carcinoma than among controls.
Poster Session II

NEOADJUVANT CHEMOTHERAPY FOLLOWED BY FERTILITY SPARING SURGERY - IS IT REALLY SAFE?

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In our prospective study (2005-2011) were included twenty patients with cervical cancer that do not fulfill standard criteria for fertility-sparing surgery (tumor more than 2 cm in the biggest diameter or infiltrating more than half of stroma). All women had strong desire to save fertility.

All patients received three cycles of dose-density neoadjuvant chemotherapy (NAC) at 10-day interval: cisplatin plus ifosfamide in squamous cell cancer or plus doxorubicin in adenocarcinoma with good tolerance. After NAC, they underwent SLNM and laparoscopic pelvic lymphadenectomy and vaginal trachelectomy.

Seven patients had no residual tumor (one of them had positive pelvic nodes), seven had only microscopic residual disease and six had macroscopic residual disease. Seven women lost fertility (radical hysterectomy - 2 decisions of patient, 4 positive endocervical margins or macroscopic residual disease, 1 had positive pelvic nodes). Fertility was spared in 13 women, eleven of them planed pregnancy and eight of them delivered 9 babies (one premature, eight term). Two women are pregnant (32nd week and 16th week of pregnancy). Four women recurred, three of them died of disease (one with positive nodes, one had recurrence in ovary, one had central recurrence).

NAC followed by fertility-sparing surgery seems to be feasible treatment for women with tumor bigger than 2 cm or infiltrated more than half of the stroma. Tumors with infiltration more than two third of cervical stroma would be excluded from protocol. When the macroscopic residual disease after NAC is present, women have high risk for recurrence.
Poster Session II

LOUPES ASSISTED NERVE SPARING ABDOMINAL RADICAL TRACHELECTOMY, AS A TREATMENT OF EARLY-STAGE CERVICAL CANCER

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The purpose of this study was to determine feasibility and safety of a novel, less morbid fertility-preserving surgery for early-stage cervical cancer patients. A loupes assisted nerve sparing abdominal radical trachelectomy was accomplished to minimize nerve plexus trauma and preservation of uterine vessels.

Between 2002 and 2011 a total of 58 radical trachelectomies with pelvic lymphadenectomy were performed. The characteristics of the patients included stage IB1 disease in all cases, a mean age of 32 years (range, 26-41) and a mean operative time of 162 minutes (range, 142-202).

Tumor diameter was ranged from 8 to 37 mm.

Uterine vessels preservation was feasible in all cases but one. There was no case with parametrial lymphnode involvement and no patient needed postoperative adjuvant treatment. Urinary and anorectal morbidity were minimal. Foley catheter was removed on the 6th day in 16 patients and on the 10th for the rest 3. Follow-up ranged from 18 to 92 months (mean 59 months).

There was 1 disease relapse on the paraortic area treated with chemoradiation. One patient developed a CIN2 lesion what was successfully treated by Loop excision. A total of 30 pregnancies (75%) were recorded from 40 women attempted to become pregnant. Of these pregnancies 19 (63.3%) were full term. There was 1 pregnancy ended at 28th week of pregnancy. All fetuses were viable.

In conclusion nerve sparing procedures by using microsurgical techniques could be applied on all fertility-preserving abdominal trachelectomies to minimize morbidity and potentially improve obstetrical outcome by preserving the uterine vessels.
Poster Session II

HIGH EXPRESSION OF TGF-β1 AND ER IN CARCINOMAS INDICATE A POOR PROGNOSIS OF PATIENTS WITH CERVICAL ADENOCARCINOMA IN STAGE I B~II A

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Objective: This study was undertaken to investigate the the prognosis significance of protein level of ERα and TGF-β1 in different glandular epithelium of cervix.

Methods: Immunohistochemistry were used to detect the protein level in the carcinomas and incisal margins of 66 cases with cervical adenocarcinoma in stage I b~II a, 20 cases of normal cervix and 20 cases of chronic cervicitis. The results was analyzed by conjugated with the clinicopathologic charateristics. Univariate and multivariate analysis were applied to evaluate the prognostic significance of the protein level of TGF-β1 and ER in the carcinomas.

Results: The expression of TGF-β1 in the carcinomas was 71.21%, significantly higher than the normal cervix(35%) and chronic cervicitis(55%)(χ²=8.901, P=0.012). Similarly, the expression of ER in the carcinomas was 68.18%, significantly higher than the normal cervix(35%) and chronic cervicitis(50%)(χ²=7.693, P=0.021). The expression of TGF-β1 and ER in the carcinomas were all seemed associate with the vaginal recurrence, infection of HPV, the depth of infiltration and lymphatic metastasis(P<0.05). Analysis of univariate and multivariate indicate that the conjugation of the TGF-β1 and ER a was an independent prognostic factor for the cervical adenocarcinom. Survival curve showed that the positive expression of both TGF-β1 and ER indicating a short lifetime of patient with cervical adenocarcinoma.

Conclusion: Protein expression of TGF-β1 and ER in the carcinomas had significant prognostic value in the patient with cervical adenocarcinoma in stage I b~II a.
Poster Session II

CERVICAL CANCER PREVENTION. THE CZECH EXPERIENCE

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The incidence of cervical cancer in the Czech Republic is app. 20/100 000 women per year. Each year, there are app. 300 death due to cervical cancer in the population of 10.5 milions. The mean age of the affected women is 49 years. This situation is mainly due to uneffective system of cervical cancer screening. The HPV vaccination seems to be one of the possible tools in decreasing the above mentioned unsatisfactory statistical items. The European registration of quadrivalent vaccine (HPV types 6,11, 16, 18) and two years of bivalent one (HPV types 16, 18). Immediately after the vaccines have been approved by Czech health care authorities and with the support of Czech Society for Gynecology and Obstetrics, the vaccination by the gynecologists and pediatricians started in the female population of 10 to 25 years. Until April 1st, 2012, the vaccination was not financially covered by insurance companies and was voluntary. The Parliament of the Czech Republic has voted a law procuring the HPV vaccination to all female population between 13 and 14 years of age covered by the insurance companies and thus free of charge.

Expected results are for the moment only speculative. The present cervical cancer vaccinated population was recruited mainly from the non risk population. We hope that all girls from 13 - 14 years of age will now a days beneficiate the whole state financial covering HPV vaccination especially those from high risk social communities. Thus an important decrease of the cervical cancer frequency can be expected.
Poster Session II

CLINICOPATHOLOGICAL IMPORTANCE OF WOMEN WITH SQUAMOUS CELL CARCINOMA ON LIQUID-BASED CERVICAL CYTOLOGY

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Objectives: The purposes of this study were (i) to determine the prevalence, (ii) positive predictive value (PPV) to detect significant neoplasia, and (iii) to evaluate the correlation between clinical and final histopathology of SCCA cytology detected by liquid-based cytology (LBC) of women in area of high incidence of cervical cancer.

Methods: The clinical and histological data of SCCA cytology of women who underwent LBC and completed investigations at Siriraj Hospital, Mahidol University from January 2007 to December 2010 were reviewed.

Results: The prevalence of SCCA cytology was 0.07 %, 86 women. Mean age was 58.14 years, 80 women (93%) were multiparous and 61 women (70.9%) were menopause. Forty women (46.5%) came to hospital for check up and 29 women (33.7%) had vaginal bleeding. Overall significant pathology and invasive cancer were 84 women (97.7%) and 71 women (82.5%), respectively. The PPV for significant pathology was 97.7%. The cervical cancer was diagnosed in 69 women, among these 58 (84%) women were squamous cell carcinoma and 26 patients were classified as early stage (I-IIA). One woman had stage IVB of vaginal cancer with cervical intraepithelial neoplasia (CIN) 3 and one had stage IVB of endometrial carcinoma. Thirteen women were CIN 3 and two women had cervicitis. Colposcopy had 83.3% sensitivity and 75% specificity for cervical cancer detection. Median follow up period was 17.6 months.

Conclusions: The final histopathological of SCCA cytology in our populations is wide variety, from cervicitis to invasive cancer and the most common diagnosis is invasive cervical cancer.
Poster Session II

LAPAROSCOPIC LYMPHOCELE FENESTRATION IN GYNAECOLOGICAL CANCER PATIENTS AFTER RETROPERITONEAL LYMPH NODE DISSECTION AS FIRST-LINE TREATMENT OPTION

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Objective: To evaluate laparoscopic lymphocele fenestration (LLF) as a first-line treatment in gynaecological cancer patients with a history of retroperitoneal lymph node dissection (LND).

Setting: A tertiary referral centre.

Population: Gyneco-oncological patients who underwent LLF between January 2001 and December 2010 following retroperitoneal LND.

Methods: Surgical outcome of 102 patients who underwent LLF at our hospital between January 2001 and December 2010 for a symptomatic lymphocele was analysed. Patients were identified using hospital database search software; hand-written and electronic charts were reviewed.

Main outcome measures: Outcomes included operating time, blood loss, conversion rate, intra- and post-operative complication rate, hospital stay and relapse rate.

Results: A total of 132 lymphoceles were fenestrated in 102 patients per laparoscopy. Mean duration of surgery was 115.6 minutes and the average intra-operative blood loss per patient was 146 ml. Overall conversion rate to laparotomy was 7.8 %. Intra and postoperative complication rates were estimated at 9.8% and 5.9% retrospectively. The rate of intraoperative and postoperative complications was significantly higher in patients after pelvic plus paraaortic LND (23.8%) compared to those after pelvic LND only (3.6 %; p>0.01). Mean follow-up time was 60.4 months and a total of seven symptomatic recurrences of lymphoceles were observed (recurrence rate: 6.9%).

Conclusion: For the treatment of symptomatic lymphoceles, LLF has been previously established as an efficient first-line treatment option in a post-transplant context. Our data suggest that these favourable results for LLF may be transferable to gynaecological cancer patients.
Poster Session II

NEOADJUVANT CHEMOTHERAPY FOLLOWED BY CESAREAN DELIVERY AND RADICAL HYSTERECTOMY FOR STAGE IB CERVICAL CANCER DIAGNOSED IN PREGNANCY: THREE CASE REPORTS


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Cervical cancer is one of the most common malignancies during pregnancy. The management of cervical cancer during pregnancy is influenced mostly by gestational age, FIGO stage of disease, and patient's desire to maintain pregnancy. We report three cases of pregnant women with FIGO stage IB cervical cancer, who were diagnosed in the second trimester of pregnancy and strongly desired continuation of their pregnancies. All patients received neoadjuvant chemotherapy with paclitaxel plus cisplatin until fetal lung maturity, and then underwent cesarean delivery and radical abdominal hysterectomy with bilateral pelvic lymphadenectomy. Histopathologic examination in all three patients showed no evidence of lymph node metastasis, no infiltration of the parametrium and clear resection margins. Two patients with intermediate risk factors such as larger tumor size, lymph-vascular space invasion, or deep stromal invasion received adjuvant chemotherapy. All three patients did not have any evidence of disease recurrence for follow-up of 12 months, 23 months, and 92 months, respectively. Pediatric follow-up of the newborn infants showed no sign of any abnormalities. In conclusion, neoadjuvant chemotherapy with paclitaxel plus cisplatin followed by radical surgery could be considered as one of feasible alternatives to primary radical surgery or concurrent chemoradiation therapy in pregnant women with FIGO stage IB cervical cancer who do not want termination of their pregnancy.
Poster Session II

CLINICOPATHOLOGICAL IMPORTANCE OF PAPANICOLAOU (PAP) SMEARS FOR THE DIAGNOSIS OF PREMALIGNANT AND MALIGNANT LESIONS OF THE CERVIX

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Background: Premalignant and malignant lesions are not uncommon in Pakistani women, especially in the older age-groups. This study was conducted to determine the clinicopathological importance of conventional Papanicolaou (Pap) smears for the diagnosis of premalignant and malignant lesions of the cervix.

Materials and methods: Pap smears of 1000 women were examined from January 2007 to June 2009. Only cases with neoplastic cytology were included.

Results: The overall frequency of normal, inadequate, neoplastic, and infective smears was 50%, 1.8%, 10.2%, and 38.3%, respectively. Most of the patients (67%) were in the postmenopausal age-group, with the mean age being 44.7±15.63 years. The commonest clinical signs/symptoms seen among the 102 patients with neoplastic gynaecological lesions were vaginal discharge and abnormal bleeding (93/102; 91.2% and 62/102; 60.7%). Of the 102 cases with neoplastic lesions 46 patients (45%) had low-grade squamous cell intraepithelial lesions (LSILs), 22 (21.5%) had high-grade squamous cell intraepithelial lesions (HSILs), 14 (13.7%) had squamous cell carcinoma, and 6 (5.8%) showed features of adenocarcinoma. Ten (9.8%) cases showed cytology of atypical squamous cells of undetermined significance (ASCUS) and four (3.9%) cases had atypical glandular cells of undetermined significance (AGUS).

Conclusion: We conclude that cervical smear examination is well suited for diagnosing neoplastic disease. It is clear that cervical neoplastic lesions are becoming a problem in Pakistan.
Poster Session II

INDEPENDENT DEMOGRAPHIC PREDICTORS OF DELAYED STAGE CERVICAL CANCER IN CALIFORNIA, 2004-2009

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Introduction: Hispanic women experience highest risk of cervical cancer (CACX) in California, followed by non-Hispanic blacks (NHB), Asian/Pacific Islanders (API), and Non-Hispanic whites (NHW). Half of California's CACX cases are delayed-stage (II-IV), with stage I (early-stage) substantially dependent upon screening.

Aims: We sought to reveal independent demographic predictors of delayed- versus early-stage CACX.

Methods: Age, race/ethnicity, socioeconomic status (SES), and marital status (MS) categories for all 8,045 stage I-IV CACX cases for 2004-2009 were extracted from the California Cancer Registry and contrast forming independent odds ratios (OR) for delayed- versus early-stage using logistic regression.

Results: ORs with 95% confidence intervals (OR, 95% CI) contrasting delayed-to-early-stage CACX for age-categories were: OR<30/50-69=0.30, 0.24-0.37; OR30-49/50-69=0.48, 0.44-0.54; and OR70+/50-69=1.37; 1.17-1.61. Contrasts for race/ethnic groups with NHWs showed: ORAPI/NHW=1.23, 1.07-1.42; ORNHB/NHW=1.13, 0.92-1.38; ORHispanic/NHW=1.07, 0.96-1.20; and ORNHB/Other/NHW=0.62, 0.40-0.96. Contrasting lower SES-categories with highest showed: ORSES1/5=1.45, 1.23-1.70; ORSES2/5=1.53, 1.31-1.80; ORSES3/5=1.23, 1.05-1.45; and ORSES4/5=1.21, 1.03-1.43 (Trend p-value=0.0001). MS contrasts of single (S); divorced, widowed, or separated (DWS); and unknown with married (M) were: ORS/M=1.41, 1.26-1.57; ORDWS/M=1.62, 1.44-1.83; and ORUnknown/M=0.72, 0.55-0.95.

Conclusions: Lower delayed- to early-stage ratio during reproductive years, with increased odds for age 70+ are consistent with Pap-screening practices. Higher delayed- to early-stage OR among APIs versus NHWs reveals inadequate screening in this, otherwise, low-risk group. The inverse dose-response discloses lower SES as a more robust predictor of delayed-stage CACX than race/ethnicity. Single and divorced, widowed or separated women experienced higher odds of delayed stage CACX than married. Further analyses of API subgroups are ongoing.
Poster Session II

DETERMINING ACTIVITIES THAT INCREASE PRESENTATION FOR CERVICAL CANCER SCREENING AND EVALUATING THEIR EFFICACY

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Purpose: Our aim in this study was to determine women's awareness and knowledge of cervical cancer and Pap smear tests and to identify the reasons for avoiding tests and the influence of women’s Pap smear screening participation initiatives' invitation methodologies on the likelihood of undergoing Pap smear testing.

Method: This interventional study was performed in 3 Turkish provinces. A total of 356 women between the ages of 30 and 65 identified with a bracket sampling method were visited at home and 3 methodologies were used to invite them for cervical cancer screening. The invitation types used were a brochure and one-on-one training, just brochure handouts and just inviting to the screening center.

Results: At the end of the study’s intervention period 55.9% of the women in the one-on-one training group, 31.9% of those who just received a brochure and 25.2% of those who were just invited presented at the centers in question to have Pap smear tests performed.

The likelihood of not having a Pap smear test done was 3.0 times (95% CI:1.73-5.36) higher among women who just received a brochure and 5.4 times (95% CI:2.92-10.18) higher than the women who were just invited in the women who received a brochure and one-on-one.

Conclusion: It is recommended that training be used in conjunction with handing out brochures to increase the Pap smear testing rate in women.
Poster Session II

A CASE OF AGE-RELATED EBV-ASSOCIATED B-CELL LYMPHOPROLIFERATIVE DISORDERS OF UTERINE CERVIX

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Introduction: Viruses highly tropic for lymphocytes have recently been implicated in the development of malignant lymphoma. Epstein-Barr viruses (EBV) are known to cause immunodeficiency and tumorigenesis with aging. We report our experience with a case of EBV-positive diffuse large B-cell lymphoma (DLBCL) incidentally detected by with pathologic investigations in the uterine cervix after hysterectomy.

Case report: A woman of 59 years old, 2 gravida 2 para, had a check-up at our hospital with a chief complaint of atypical genital bleeding lasted for two years. Magnetic resonance imaging revealed only a 6-cm solid mass in the left adnexa, but computed tomography showed no lymphadenopathy. We performed simple total hysterectomy and bilateral salpingo-oophorectomy, because of the possible presence of ovarian malignancy and an uterine primary lesion. Although the left ovarian tumor was pathologically diagnosed as a benign Brenner tumor, a focal proliferation of atypical lymphocytes was observed in the cervix of the resected uterus. Immunophenotyping was positive for both CD20 and CD79a, and for EBV antibody. A diagnosis of age-related EBV-associated B-cell lymphoproliferative disorder (aEBVLPD) in uterine cervix was finally rendered. The patient underwent adjuvant chemotherapy at the department of hematology and is with no signs of recurrence.

Conclusion: aEBVLPD is a disease group characterized by DLBCL in elderly without predisposing immunodeficiency, and increasingly occurs with age. It may be of insight to take note that aEBVLPD may incidentally be encountered associated with gynecologic disease.
PHOTODYNAMIC THERAPY FOR RECURRENT OR RESIDUAL UTERINE CERVICAL CANCER AFTER CONIZATION

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Cervical conization has been widely used as the uterine preservation treatment for the cervical cancer in the early stage up to stage Ia. In the case of recurrent cervical cancer after conization or in the case of residual cancer with positive surgical margin of the cone, either simple total hysterectomy or the 2nd cervical conization is usually performed. However, if the 2nd conization is performed when hoping fertility preservation, the possibilities of premature delivery are thought to become high because of shortened cervical length. Therefore, we performed PDT for the case of recurrent or residual cervical cancer after conization to evaluate its response rate and clinical outcome. PDT was performed with informed consent to 33 cases of recurrent or residual cervical cancer after conization under the diagnosis of severe dysplasia (n=6), CIS (12), AIS (1) and stage Ia cervical cancer(14). The excimer-dye laser irradiation was performed using colposcopy and endocervical probe at 100J/cm² 48 hours after intra-venous administration of Photofrin at 2mg/kg. 31 out of 33 cases of recurrent and residual cervical cancer who underwent cervical conization showed CR after PDT (CR rate: 94%). No case of re-recurrence after CR has been observed so far. Observation period ranges from 1.5 through 16 years after PDT. Furthermore, 6 among 29 cases hoping fertility preservation resulted in pregnancy and delivered 8 healthy babies. Although the further accumulation of cases is required, PDT is considered to be a useful uterine preservation therapy even for postoperative recurrence and residual cancer after cervical conization.
Poster Session II

NEOADJUVANT TRANSARTERIAL CHEMOEMBOLIZATION (TACE) FOR LOCALLY ADVANCED CERVICAL ADENOCARCINOMA


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Objective: Adenocarcinoma (including adenosquamous carcinoma) of the uterine cervix has a tendency of early lymph node metastasis and is resistant to radiation therapy, thus results in poor prognosis compared with squamous cell carcinoma. Neoadjuvant chemotherapy (NAC) followed by radical hysterectomy (RH) for bulky cervical adenocarcinoma seems to be an alternative therapy instead of primary radiation.

Methods: The NAC regimen consisted of paclitaxel (60 mg/m², iv, Days 1, 8, and 15) and cisplatin (70 mg/m², TACE, Day2) repeated every three weeks for 3 cycles, followed by RH. Primary endpoint was clinical and pathological response, and secondary endpoints were progression free survival (PFS) and overall survival (OS).

Results: Enrolled patients: 22 (1998-2006), Age: median 51 (33-75), FIGO stage: IB2(9), IIA-IIIB(8), IIIIB(3), IVA(2), Adeno/Adenosquamous: 16/6. Clinical response rate (RR: CR+PR) of the patients with IB2/IIA-IIIB were 100%, 16 out of 17 were completed RH, and no residual malignant cells were found pathologically (pCR) in 3 out of 17 (18%) patients. Both 5 year PFS and OS were 70%. One of three patients with IIIb achieved PR and completed RH. Their PFS were 104, 16, 13 months, and OS were 104, 35, 34 months. The results of two patients with stage IVA were as follows: CR (1), PR (1); pCR (1). RH were carried out with anterior or posterior exenteration, and no radiation therapy were performed. They are alive with no evidence of disease for 110 and 72 months after the entry.

Conclusions: NAC with TACE for cervical adenocarcinoma was highly effective.
**Poster Session II**

**SEXUAL FUNCTION AFTER NEOADJUVANT CHEMOTHERAPY AND FOLLOWED BY TYPE III RADICAL HYSTERECTOMY FOR LOCALLY ADVANCED CERVICAL CANCER**

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**Introduction:** Surgical treatment for cervical cancer is associated with a high rate of late postoperative complications, and in particular with sexual dysfunction.

**Aim:** To evaluate sexual function in women who underwent neoadjuvant chemotherapy (NACT) followed by type III radical hysterectomy (RH).

**Methods:** We have enrolled in the oncologic group (OG) sexually active patients affected by cervical cancer (stage IB2 to IIIB) treated with NACT followed by RH between 2007 and 2011. Two consecutive assessments were recorded: at the first evaluation postoperatively (T1) and at the 8-month follow-up visit (T2). **MAIN OUTCOME MEASURES:** (Female Sexual Function Index) FSFI questionnaire on six domains of female sexuality (desire, arousal, lubrication, orgasm, satisfaction, pain). Results were compared with a benign gynecological disease group (BG) and with a healthy control group (HG).

**Results:** A total of 38 patients for OG, 41 for BG, and 38 women for HG were recruited. After surgery, sexual activity has been resumed by 48% of the OG patients and 65% of the BG patients (P = significant). For sexual activity, the score difference between cancer survivors and women with benign gynecological disease is statically significant.

**Conclusion:** Considering the high rates of sexual dysfunction and sexual inactivity, there is a need to integrate sexuality into routine nursing care.
Poster Session II

TREATMENT OUTCOME IN LOCALLY ADVANCED CERVICAL CANCERS - CANCER INSTITUTE, CHENNAI, INDIA EXPERIENCE

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Objective: Retrospective analysis of different treatment modalities and radiotherapy techniques in the treatment of locally advanced cervical cancers and its relation to disease free survival (DFS) and treatment related complications.

Methods: A total of 4556 cases of locally advanced cervical cancers who were treated from 1995 to 2004 at our institute were analyzed, treatment modalities like only radiation (with or without brachytherapy), chemo radiation and different radiotherapy techniques like 4 field box, conformal and IMRT techniques were also analyzed.

Results: Most of the patients (68 - 70%) were stage II and III. Complete followup at 5 years was 90%. DFS at 5 and 10 years were 62% and 54% for stage IIB and 45% and 35% in stage III. External beam radiotherapy alone showed a very poor DFS of 35% at 5 years, the addition of brachytherapy and chemotherapy increased the survival significantly (58%). Comparing different radiotherapy techniques an anterior placed 5 field conformal technique showed less rectal toxicity than 4 field box technique (Gr II - III complications 8% and 15% respectively) when combined with chemotherapy (weekly CDDP). Hematologic complications and bone marrow toxicity was reduced with conformal technique (V20 less than 70%) this favoured completion of treatment without delay. IMRT technique is better than 4 and 5 field technique when the complications are considered (Gr II - III rectal toxicity < 5%) and DFS was not statistically significant.

Conclusion: In a developing country like India, our data showed careful pretreatment planning and treatment with chemo radiation will be the recommended treatment for locally advanced cervical cancers.
Poster Session II

**ROBOT ASSISTED LAPAROSCOPIC RADICAL HYSTERECTOMY VERSUS ABDOMINAL RADICAL HYSTERECTOMY WITH BILATERAL PELVIC LYMPHADENECTOMY FOR TREATMENT OF EARLY STAGE CERVICAL CANCER**

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**Objective:** To compare the feasibility, morbidity and survival outcome of the robot assisted laparoscopic radical hysterectomy and bilateral pelvic lymphadenectomy (RALRH+RBPLA) with abdominal radical hysterectomy and bilateral pelvic lymphadenectomy (ARH+ABPLA) for FIGO stage IA2-IB1 cervical cancer patients.

**Methods:** The consecutive cases with FIGO Stage IA2-IB1 cervical cancer from November 2005 to October 2011 were documented, including 60 patients underwent RALRH+RBPLA, and 120 patients underwent ARH+ABPLA as control group. The clinic data of perioperative periods and survival were compared between the groups.

**Results:** In robot assisted laparoscopic group the operating time increased 264.2 min. vs 169.6 min, p=0.203 and resected number of pelvic lymph nodes decreased 26.4 vs 20.4, p=0.840. No significant difference was found between groups. On the other hand Estimated Blood Loss(EBL) during operation 83 ml vs 457 ml, p=0.0001. Postoperative length of hospital stay (LOS) 3.6 days vs 9.1 days, p=0.0001. Significant difference was found between groups regarding EBL and LOS.

All robot assisted laparoscopic procedures were completed successfully and no cases was converted to laparoscopy. The median follow-up was 52 months (4-80) in open and 36 months (5-78) in robot assisted group. No cases lost to follow-up. The recurrence rate 9.1 % in open vs 8.3 % in robot assisted group, p>0.05.

**Conclusions:** Our data demonstrated that cervical cancer could be treated successfully with robot assisted laparoscopic radical hysterectomy and bilateral pelvic lymphadenectomy with similar efficacy and recurrence rates to ARH+ABPLA. RALRH+RBPLA is a safe and effective alternative to conventional abdominal surgery.
**Poster Session II**

**EFFICACY AND TOXICITY OF CONCURRENT CHEMORADIOTHERAPY WITHOUT BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER: A CLINICAL TRIAL PHASE II**

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**Objective:** Concurrent chemoradiotherapy plus brachytherapy is the standard of care in patients with advanced cervical cancer. However, some patients are unable to undergo brachytherapy. In this study, we evaluated the treatment outcome in patients with locally advanced cervical cancer undergoing conventional EBRT plus weekly chemotherapy.

**Method:** We selected patients with locally advanced cervical carcinoma undergoing external beam radiotherapy and chemotherapy without brachytherapy between 2007 and 2009. The patients received 50 Gy in 5 weeks to whole pelvic followed by a localized boost dose on tumor to 70 Gy concurrently with cisplatin 35 mg/m² weekly. The treatment related toxicities and survival were evaluated.

**Results:** 30 cases with a median age of 55 were studied. The Clinical stages were as follows: stage: IIB 23, IIIA 4, and IIIB 3 cases. Three months after treatment, 19 patients (63.3%) achieved complete response. With a median follow up time of 18 months, 8/23 cases (34.7%) with stage IIB and 2/7 (28.5%) among stage IIIA-IIIB remained disease free at the end of follow up. 2-year overall survival rate was 58.7% ± 9% and 2-year disease free survival was 37.7% ± 9%. Most toxicities were grade I and II. 4 (13.3%) grade III, IV diarrhea and 4 (13.3%) grade III neutropenia were recorded.

**Conclusion:** Although, in locally advanced cervical cancers using modern radiation therapy techniques with increased delivered boost dose might improve treatment results. However, in centers that the modern radiation therapy techniques are unavailable, continuing chemo-radiotherapy to 70 GY is acceptable and might be curative in some patients.
Poster Session II

CLINICAL RESEARCH ON THE TREATMENT OF CERVICAL CARCINOMA WITH THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY - AN ANALYSIS OF 50 CASES

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Objective: To explore the clinical effect of the treatment of cervical carcinoma with three-dimensional conformal radiotherapy (3DCRT) and compare with traditional radiotherapy.

Methods: Totally 50 cases of cervical carcinoma were treated with 3DCRT, and select 30 cases at the same period as the control group. Observe the short-term treatment effect and acute reaction in both groups.

Results: The short-term effective rates of the treatment group and the control group were respectively 96% (27/28) and 97% (29/30), with no significant difference \( (P>0.05) \). The effective rates of patients with recurrence or metastasis were respectively 92% (12/13) and 77% (7/9). The rate of acute radiation reaction of the rectum between the treatment group and control group were respectively 46% (13/28) and 80% (24/30), with significant difference \( (P<0.05) \). The rate of bone marrow depression between two group were respectively 71% (20/28) and 63% (19/30), with no significant difference \( (P>0.05) \), but the rate of severe bone marrow depression between two group were with significant difference (respectively 0% and 13%, \( P<0.05 \)). The rates of acute radiation reaction of bladder between two group were respectively 7% (2/28) and 3% (1/30), with no significant difference \( (P>0.05) \).

Conclusion: The therapeutic effect of 3DCRT was similar to that of traditional radiotherapy in the treatment of cervical carcinoma, but the former treatment method had a lower rate of acute complications.
Poster Session II

ABDOMINAL RADICAL HYSTERECTOMY VERSUS TOTAL LAPAROSCOPIC RADICAL HYSTERECTOMY FOR EARLY STAGE CERVICAL CANCER

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Objectives: Increasingly, early stage cervical cancer is now being managed laparoscopically by performing Total Laparoscopic Radical Hysterectomy (TLRH). Traditionally, Abdominal Radical Hysterectomy (ARH) has been the standard approach. We evaluate our first 10 cases of TLRH compared with ARH within our institution, a UK cancer centre.

Methods: A retrospective data review from patient notes and hospital computer records of 22 patients with early stage cervical cancer (1A2 to 1B2) treated by either ARH or by TLRH over a period of 6 months (May 2011 and December 2011).

Results: In the ARH group versus the TLRH group blood loss was significantly greater (3.55g/dl vs 1.55g/dl) p=0.02, and hospital stay significantly longer (5.83 days vs 2.9 days) p=0.004.

The average operating time was 153mins for TLRH vs 128mins for ARH (p=0.02)

There appears to be no significant difference between average lymph node count and vaginal cuff length between the groups. The TLRH group were less likely to require blood transfusion, return to theatre or have wound complications. They were however more susceptible to postoperative urinary retention

Conclusion: Despite the small number of cases reviewed, TLRH appears a suitable alternative to ARH for the treatment of early stage cervical cancer with significant decrease in hospital stay and intra-operative blood loss. Other than post-operative urinary retention, there was overall decreased morbidity from TLRH group.
Poster Session II

ROLE OF ANGIOGENIC MARKERS AND LAMININ IN POST TREATMENT (NEOADJUVANT CHEMORADIATION) DISEASE MAPPING IN ADVANCED STAGE CARCINOMA OF UTERINE CERVIX

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Background and aims: Carcinoma of uterine cervix accounts for most common malignancy in Indian women. Currently chemo-radiation is mainstay of treatment. Post treatment (Neoadjuvant Chemotherapy) disease mapping using angiogenic factors and Laminin in carcinoma cervix patients needs to be explored. Comparing circulatory and cellular levels of VEGF, Ang-2 & Laminin in patients with stage III carcinoma cervix, with those of healthy women & further to evaluate effect of chemo-irradiation on their levels.

Methods: 40 patients of cancer cervix stage IIIb were recruited. Circulatory levels of VEGF, Ang-2 & Laminin were measured before treatment, after chemotherapy & teleradiation, using ELISA and correlated with therapeutic response. mRNA levels were quantitated using Q-PCR and statistically analyzed.

Results: VEGF, Ang-2 and Laminin levels of patients were significantly (p< 0.001) higher than in controls. There was also a significant (p< 0.001) decline in levels of VEGF, Ang-2 and Laminin after treatment when compared to before treatment levels. Out of 40 patients, 33 were complete responders and 7 were non-responders when they were clinically assessed. On comparison of before and after treatment levels of VEGF, Ang-2 and Laminin, complete responders showed significant decline whereas non responders showed insignificant decrease in their levels.

Conclusions: Higher levels of angiogenic factors indicate role played by them in disease progression aiding angiogenesis. It may be possible that these angiogenic factors function via up-regulation of matrix proteins (laminins). These markers may serve as useful tools in post treatment disease mapping which otherwise may not provide true picture with available imaging methods.
**Poster Session II**

**PET SCAN FOR PREDICTING CLINICAL OUTCOME OF PATIENTS WITH RECURRENT CERVICAL CARCINOMA FOLLOWING RADIATION THERAPY**

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**Aim:** To evaluate the role of positron emission tomography (PET) for predicting the clinical outcome of patients with recurrent cervical carcinoma following definitive radiation therapy (RT).

**Patients and methods:** Twenty two patients of post irradiated recurrent cervical carcinoma (PIRCC) were enrolled in this prospective study. 18-fluorodeoxyglucose (FDG) PET imaging was performed in each patient before the salvage therapy. The maximum Standardized Uptake Value (SUVmax) and metabolic tumor volume (MTV) were measured and correlated with cumulative progression free survival (PFS).

**Results:** Median age of patients was 42 years. Majority of patients had stage III disease at the initial presentation and all 22 patients had received prior definitive RT. The median recurrence free period was 11 months. Salvage therapy consisted of surgical resection, re-irradiation or palliative chemotherapy depending upon the various clinical and radiological factors. Median SUVmax was 5.8 (range 1.8-50.6) and median MTV was 43 cm³ (range 5.8-243). The cumulative PFS for all patients was 20% at 30 months. The 1-year PFS was 28% for patients with SUVmax value of $>5.8$ versus 42% for those with SUVmax value of $< 5.8$ ($p$ value 0.01). The 1-year PFS was 43% for patients with MTV value of $>43$ cm³ versus 45% for those with MTV value of $< 43$ cm³ ($p$ value 0.8).

**Conclusion:** Our results have suggested that FDG uptake on PET scan can predict the clinical outcome of PIRCC patients. Further randomized studies may be conducted with large sample size and longer follow up to establish its definite predictive value.
Challenge in Developing Countries to Cure the Incurable Beyond FIGO/TNM Cancer Cervix Stage: Balanced Chemoradiation Techniques

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Background and aims: Unsatisfactory volume quantification in FIGO staging results in palliation or under treatment to massive tumor volumes. Inadequate expertise, experience and information on treatment aggression has affected cure in deserving patients. Late stage cancer cervix constitutes 80% and is a challenge to Indian gynec oncologist. The aim of this study is to cure the incurable advanced cancer cervix patient using balanced chemoradiation technique.

Methods: IIB/IVA FIGO CT/MRI assessed cancer cervix (tumor quantification) frozen pelvis or less intact ureteric/rectal patency.

Therapeutic Protocol:
- Response based Neo Adjuvant Chemotherapy (NACT),
- Chemoteleradition: image evidenced paraaortic also
- Chemosensitized brachytherapy
- Adjuvant Chemotherapy,
- Long-term Ayurvedic Immuno boosters Septilin and Immumo
- Rigorous follow up

Results: Symptom Relief: The instantaneous symptomatic relief (Third day) 90%

Response and Regression: 80% Total virtual regression after second NACT, 70% Normal Anatomy.

End of Teletherapy: 95% fit for standard or modified brachytherapy application.

Post Radiation therapy/ Adjuvant chemotherapy: 70% cases tolerated two courses while only 50% could tolerate third course.

Long term (10 year) survivals:

Stage III Bulky Disease (Radiological volume more that 60 CC) 70% with 20% inter-current death.
Stage IV Bulky Disease 60% with inter-current / metastatic recurrences 20%, local recurrence 10%

Pattern of Local Recurrence: Mainly parametrial/ late metastatic

Sequelae of treating massive disease -Management of massive replacement by fibrosis and massive destruction of the disease.

Conclusion: Judicious treatment aggression on late stage bulky cancer cervix can convert palliative approach into curative approach. Ayurvedic Immunostimulants have significant role to play.
HAEMOSTATIC CHEMOTHERAPY IN BLEEDING CANCER CERVIX
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Background and aims: Haemostatic chemotherapy seems to be sure answer for bleeding advanced stage cancer cervix patients when radiotherapy or interventional radiology is not instantaneous. The aim of this study is to achieve effective haemostasis and long term survival in these patients.

Methods: 60 fresh uncontrolled bleeding cancer cervix cases (IIB/ III and IV A) were included in this study. The retronalysis was divided in two groups,

· A (n=30) Haemostatic RT (300 Cgy- 450 Cgy in 3/2 fractions)
· B (n=30) Hemostatic Chemoinfusion- (5Fu 350mgD1-5 CDDP30mg D1-4 BLM 10 mg D1&D5 /m²)

Endpoint haemostasis, Symptomatic Relief, Tumour Regression, Bowel/Bladder symptomatology and Confidence were observed.

Results: “The Ill Day “:

· Startling instantaneous haemostasis in 90% of Chemogroup as compared to 50% in RT group.
· Pain relief in 70% in chemo group when compared to 20% in RT Group.
· Rise of Hemoglobin to 10 gms%. Hemostatic Chemotherapy group 80%. RT group 30%.
· Long-term survival for this locally advance disease was 60% for Chemo group (Neo Adjuvant and Post RT Adjuvant) as compared to 25% in RT group that initiated as palliative RT - proceeding to complete RT.

Conclusion:

Advantages Haemostatic Chemotherapy: As low Hb as 6 gm% can be given. All time available “Chemo” continues to achieve tumour regression that helps core extirpation. Resultant reduction in Brachytherapy dose.

Poster Session II

COMPARATIVE STUDY OF VAGINAL VS. ABDOMINAL RADICAL TRACHELECTOMY FOR EARLY STAGE CERVICAL CANCER: PRELIMINARY REPORT OF MULTI-CENTER RESEARCH IN CHINA

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Objectives: To compare the surgical and pathologic characteristics, the prognosis and fertility outcomes of the two surgical approaches.

Methods and materials: 10 centers in China participate in this study. Total 125 cases enrolled according to our criteria and data completed in 115 cases including 71 cases in VRT group and 44 cases in ART group.

Results: There was no significant difference statistically in general characteristics of the patients, tumor state before treatment, operating time, blood loss and complications. In ART group, 2.3% had margin positive, 4.5% had LVSI, 4.5% had lymph nodes positive and 2.6% had parametrium invasion. In VRT, 2.8% had margin positive, 4.2% had LVSI and no patients had lymph nodes and positive parametrium invasion (p>0.05). During the mean follow up of 16±8 months in ART group, no patient developed recurrent diseases, however in VRT group, during the mean follow up of 27±18 months 5.6% patients developed recurrent diseases and 2.8% patients died of the tumors (p<0.05). In VRT group the rate of pregnancy was 15.7% with 7.2% live birth rate, however in ART group the rate of pregnancy was 2.4% with no live birth (p<0.05). Tumor size (>2cm) is a poor prognostic factor for recurrence (p<0.05).

Conclusions: Vaginal or abdominal radical trachelectomy provides similar surgical and pathologic outcomes. Patients treated by ART obtained better prognosis, but patients treated by VRT had better fertility outcome. Tumor size < 2 cm should be emphasized as an indication for radical trachelectomy for improving the outcome of fertility and prognosis.
Poster Session II

IMPACT OF ASYMMETRIC SIZED OVOIDS ON INTRACAVITARY BRACHYTHERAPY DOSE DISTRIBUTION FOR CARCINOMA CERVIX

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Aims: To evaluate and compare the dose distribution in Intracavitary Brachytherapy (ICBT) by using asymmetric ovoids in same patients for different sessions.

Methods: We prospectively analysed point based dosimetric distribution data for 11 sessions of carcinoma cervix for which asymmetric ovoids were used during one of the sessions. Asymmetric ovoids were tried due to distorted anatomy of the patient. CT based ICBT planning was done, point A, B, ICRU 38 rectal and bladder doses along with lateral fall off was analysed.

Results: Dose received by ICRU 38 rectal and bladder points were almost similar. Asymmetric and symmetric pear shaped distribution is shown in figure 1(a), 1(b) respectively. As it is obvious from the figure 1(a) 100% isodose line is reaching up to 3 cm on right side (diseased side) from the flange whereas in figure 1(b) it is up to 2.5 cm on the right side from the flange.
Conclusion: Use of asymmetrical ovoids can be considered as an option for distorted anatomy patients without influencing bladder and rectum doses.
Poster Session II

SHORT- AND LONG-TERM OUTCOMES AFTER COMPREHENSIVE ROBOTIC SURGICAL STAGING FOR CERVICAL CANCER

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Aims: To assess surgical and survival outcomes after robotic surgery for cervical cancer.

Methods: Consecutive women with early stage cervical cancer (FIGO stages IA2-IB1) and patients responders to neoadjuvant chemotherapy for locally advanced cervical cancer (FIGO IB2-IIB) were considered eligible for this retrospective study. Women were submitted to Type C1 radical hysterectomy and pelvic lymphadenectomy with a Da Vinci Surgical System at a single institution.

Results: Starting from November 2007, 47 women received comprehensive surgical staging for cervical cancer. Twenty-nine (61.7%) and 18 (39.3%) women had an early stage and a locally advanced condition, respectively. Operations were performed in 246 (range 138-380) minutes with 100 (range 50-600) ml of estimated blood loss. The median length of parametria and vaginal cuff were 30 (range 10-55) and 20 (range 10-60) mm, respectively, with 22 (range 12-66) pelvic lymph nodes retrieved. One (2.1%) patient required blood transfusion. Neither intraoperative complications nor conversions to laparotomy occurred. Early and late post-operative complication were recorded in 2 (4.2%) and 3 (6.3%) women, respectively. After a median follow-up of 22.4 (range 3-53) months 3 (6.3%) women had a recurrence. No cancer-related deaths were so far recorded.

Conclusions: Robotic surgery represents a viable option to properly perform a comprehensive surgical staging for cervical cancer for both early stage and locally advanced conditions with a low complications rate. Longer follow-up is needed to establish definitive conclusions on survival.
PROGNOSTIC FACTOR ANALYSIS, SURVIVAL AND PATTERNS OF FAILURE IN FIGO STAGE 3 SQUAMOUS CELL CANCER OF THE CERVIX

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Purpose: To further characterise FIGO stage 3 cervix cancer patients with squamous cell carcinoma (SCC) using MRI and PET.

Methods: The tumour volume, corpus invasion, parametrial extension, ureteric obstruction and nodal involvement were assessed using MRI and PET in 118 patients with FIGO stage 3 cervical SCC between 1996 and 2008.

Concurrent chemo-radiotherapy with curative intent was used in 91/118 patients. Prognostic factors were examined in relation to patterns of failure and survival using uni and multivariate cox proportional hazards models. Data was collected prospectively.

Results: Seventeen percent of patients were FIGO stage 3A and 83% were FIGO stage 3B. Parametrial involvement was present in 87% of patients. Node positivity and corpus invasion was observed in 65% and 85% of patients respectively. Median(IQR) tumour volume was 65(34-101)cc.

Patients treated curatively had a median follow-up of 46 months. Overall survival(OS) and Failure free survival(FFS) at 60 months was 45% and 46% respectively.

Backward stepwise model selection showed MRI tumour volume (HR, 95%CI: 1.6, 1.04-2.08) and ureteric involvement (HR, 95% CI: 1.8, 0.96-3.36) were predictive of OS. For FFS, volume (HR, 95%CI: 1.6, 1.04-2.35) and nodes (HR, 95% CI: 1.7, 0.85-3.51) were predictive. Local, pelvic, para-aortic and distant failure rates were 23%, 32%, 36%, and 33% respectively. Most patients failed in multiple sites except one solitary local recurrence.

Conclusions: In FIGO stage 3, SCC cervix treated with chemo-radiotherapy, increasing MRI tumour volume, presence of ureteric obstruction and metastatic nodes were significant predictors of survival. Parametrial extension in particular had no prognostic significance.
Poster Session II

TITLE- COMPARATIVE STUDY OF PREINVASIVE AND INVASIVE LESIONS OF CERVIX IN HIV POSITIVE AND HIV NEGATIVE WOMEN

N. Singh, U. Singh, A.K. Tripathi, S. Qureshi, B. Bansal, HIV positive Women and seronegative Women

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Title- Comparative study of preinvasive and invasive lesions of cervix in HIV positive and HIV negative women.

Aims and objectives: To find the incidence of preinvasive and invasive cervical lesions in HIV positive women · To compare the disease characteristics and demographic profile with HIV negative women.

Materials and methods: This cross-sectional study was done in Department of Obstet & Gyne at CSM Medical University, Lucknow, India. HIV positive cases (80) were taken from ART clinic and controls (95) from gynecology outpatient. Women with past history of cervical neoplasia, hysterectomy, other immunosuppressive diseases and unmarried women were excluded. Institutional ethics committee approval was taken. All women had Pap smear followed by colposcopy and guided biopsy for abnormal reports. Sociodemographic parameters and type of the cervical lesions were recorded. Data analysis was done on windows 2007 to compare cases and controls.

Results: Incidence of cervical lesions in cases (250/1000) was significantly higher (p< 0.001) than in controls (21/1000). HIV positive cervical lesions were asymptomatic in 93.7% while HIV negative controls were symptomatic in 73.8%. 70% of HIV positive cervical lesions were seen before 40 years. HIV positive women with cervical lesions had ASCUS(10), LSIL(05), HSIL(03), and Sq Cell CA (1) detected while the 2 controls with cervical lesions had ASCUS only.

Conclusion: Incidence of cervical lesions in HIV positive women is significantly higher than HIV negative women and they occur at a younger age without any symptoms. Thus, cervical screening in HIV positive women must be started with the detection of HIV infection and done more frequently.
Poster Session II

CHEMORADIATION IN LOCALLY ADVANCED CERVICAL CANCER (LACC)


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Objectives:

1. To assess the response of chemotherapy and chemoadjuvant radiotherapy in patients with locally advanced cervical cancer.
2. To analyze side effect profiles of chemotherapy & chemoadjuvant radiotherapy.
3. Observe the contribution of chemotherapy in increasing locoregional and systemic control of the disease.
4. Evaluate a new mathematical model to help compare results of various clinical studies.

Materials: Prospective, randomized phase 3 trial in a tertiary care University hospital in South India. One of the largest randomized studies of its type, 120 patients with locally advanced cervical cancer (40 stage IIb, 80 stage IIIB) were randomized to receive 2 cycles of Cisplatin, Vincristine and 5-Fluorouracil followed by radiotherapy or radiotherapy alone and the responses were assessed.

Methods: Prospective randomized study.

Standard statistical analysis including regression analysis used.

Results: Patients with good clinical responses to chemotherapy responded to subsequent radiotherapy. Clinical stage, tumor size & burden had an inverse relationship to clinical response. Nausea/vomiting and alopecia were the major side effects of chemotherapy. Diarrhea, local skin reaction and alopecia were the major side effects of radiotherapy. Our modified score was a better indicator of response compared to previous ones.

Conclusions: Chemoadjuvant radiotherapy is safe in the combination used in this protocol. This may have a role in patients with large tumor burdens and in patients who are inherently better responders to this treatment. Further research is needed to determine this subgroup of patients. Hopefully, for most people widespread education, vaccination and screening will help decrease the morbidity from cervical cancer.
Poster Session II

EVALUATION OF DIFFUSION WEIGHTED IMAGING IN LOCALLY ADVANCED CARCINOMA OF CERVIX TREATED BY NEOADJUVANT CHEMOTHERAPY FOLLOWED BY CHEMORADIATION

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Background: Diffusion Weighted Imaging (DWI) has the potential to differentiate cancerous from normal tissue. We studied the predictive capability of DWI in locally advanced cervical cancer treated by dose dense neoadjuvant chemotherapy (NACT) prior to standard concurrent chemoradiation (CRT).

Methods: Between June 2010 and February 2012, 28 patients (median age - 52 years, range 35 - 67) with locally advanced cervical cancer received NACT using paclitaxel and carboplatin weekly for 6 doses followed by CRT. Conventional and DWI/ADC (Apparent Diffusion Coefficient) MRI were done before and at week 24 of treatment.

Results: Baseline stages were: stage 2A - 17.8%, 3B - 71.4%, 4A - 10.7%. One patient defaulted during CRT. Twenty-four patients (pts) completed treatment of which 23 were in CR and 1 in PR. At a mean follow up 7.4 months (range 2 - 18), 85% pts were in CR, 3.7% in PR, 7.4% in PD and 3.7% relapsed. Acceptable Grade 3/4 hematologic and non-hematologic toxicities were observed during NACT and CRT. The mean ADC of cervix mass/cervix increased from a baseline value of 0.8±0.11 x10⁻³ mm²/s to 1.48±0.86 x10⁻³ mm²/s at week 24 (p= 0.03). No relation of ADC to achievement of CR status (p=0.5) was seen but a negative association was observed with low baseline serum albumin (p=0.003) and hemoglobin (p=0.029) levels.

Conclusions: In locally advanced cervical cancer, NACT with weekly paclitaxel and carboplatin followed by CRT gives a high response rate. Low baseline serum albumin and hemoglobin levels, but not DWI, are useful in predicting outcome.
Poster Session II

SENTINEL LYMPH NODE STATUS IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCERS AND IMPACT OF NEOADJUVANT CHEMOTHERAPY

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Objectives: Neoadjuvant chemotherapy (NAC) is used in locally advanced cervical cancers with the aim to decrease the size of the tumor and to allow for less radical surgery. Despite of the fact that the high response rate of the tumour has been well established, the impact of NAC on sentinel lymph node (SN) detection and status has not been explored to date.

Methods: Our study included 82 patients with locally advanced cervical cancers (FIGO IB1 >3 cm, IB2, IIA2 and selected IIB) out of which 51 patients were referred to SN biopsy prior to NAC and 31 patients to radical surgical procedure including SN biopsy after three courses of “dose density” NAC. In both groups, the prevalence of macrometastases, micrometastases and isolated tumor cells (ITC) in SN were compared.

Results: The total of 179 SNs were evaluated. SN detection rate in the whole cohort reached 87.8% per patient and 60.9% bilaterally, without significant difference between both groups. In the group with upfront SN biopsy prior to NAC the prevalence of macrometastases, micrometastases and ITC amounted to 43.1% (22/51), 7.8% (4/51) and 7.8% (4/51) respectively. In the group with SN biopsy after previous NAC, macrometastases were detected in 22.6 (7/31) of patients in SN, whereas there was only one micrometastasis and no ITC detected in that group.

Conclusions: Neoadjuvant chemotherapy did not influence the detection rate of SNs, yet it was associated with significantly reduced prevalence of metastatic involvement of SNs, especially almost completely eliminating low volume disease.
Poster Session II

NEUROENDOCRINE CARCINOMAS OF UTERINE CERVIX (N.C.U.C.): REVIEW OF OUR EXPERIENCE ABOUT THE CLINICAL MANAGEMENT AND TREATMENT

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Objectives: To present our experience in the clinical management and treatment of NCUC.

Material and methods: Retrospective and descriptive study. There were included 5 patients with small cells NCUC, over 2420 cervical cancers (0.20%) between years 2000-2010. Age, clinical presentation, FIGO stages, type of treatment and follow-up were analyzed.

Results: Mean Age: 48 (33-61) years old. Clinical presentation: 100% had genital bleeding, and 1 (20%) micturation disturbances.

Pathological findings:

1 case (20%) NCUC G1, and 4 (80%) G3. FIGO stages: 1 Ib2, 3 IIIb and 1 IVa with bilateral parametrial involvement and bulky central tumor >7 cm.

The treatments were:

1 case (Stage IIIb) of platinum-based concurrent chemotherapy + radiotherapy;

2 cases (1 Stage Ib2 and 1 IIIb) of platinum based neoadjuvant chemotherapy (NCH) followed by radical hysterectomy, postoperative adjuvant chemotherapy, and whole pelvic irradiation; and 1 case of palliative chemotherapy (stage Iva). In the NCH cases, were found complete pathological responses. One patient died (20%, the stage Iva case). The other ones are free of disease. Follow-up: 16,2 (2-28) months.

Conclusions: The low number of cases reported in the literature makes difficult to standardize the therapeutical strategies. Neoadjuvant chemotherapy could be taken into consideration as an available treatment in selected patients.
**Poster Session II**

**HPV-DNA EVALUATION IN LSIL FOLLOW-UP**

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**Objective:** The aim of this retrospective study was to assess the persistence of specific HPV types at the 18 months follow-up in women with LSIL cytology.

**Material and methods:** The study included 91 women with ages between 18 and 53 years with LSIL cytological findings, selected from a group of 604 women enrolled in a cervical screening project. These patients were reassessed at 18 months by cytology and HPV DNA genotyping. Cervical cytological grading respected the Bethesda guidelines. Nucleic acid extraction from cervical swabs used Qiagen kit. All 91 women were examined with the use of molecular test Linear Array Roche Diagnostics, which detects 37 high- and low-risk human papillomavirus genotypes, including those considered a significant risk factor for HSIL progression to cervical cancer.

**Results:** Out of the 91 LSIL women, 59 were HPV HR positive in single or co-infections. During follow-up 27.7% of patients presented type specific HPV-HR persistence (types 16, 51, 18, 39, 66), while 23.8% cleared the infection (types 16, 31, 35, 66). After 18 months over 70% of women had lower cytological grades (28.6% ASCUS and 42% NILM, especially women under 35 years of age), while 24% still had LSIL and 4.5% progressed to HSIL.

**Conclusions:** HPV-DNA genotyping test can delineate specific types. Thus, we consider them more suitable to detect persistent infection. Analysis of persistence of individual types could not be cross-examined by statistics as our type specific data were limited. However, some HPV types appeared to be easier to remove than others.
**Poster Session II**

**EFFECT OF THE AMILORIDE ON THE EXPRESSIONS OF MATRIPASE, UPA, UPAR AND MMP-2 MRNAS IN HUMAN CERVICAL CANCER CELL IN VITRO**

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**Objective:** To investigate the effects of Amiloride, which is the synthetic inhibitor of urokinase plasminogen activator, on the expressions of Matriptase, uPA, uPAR and MMP-2 mRNAs in Vitro.

**Methods:** After treated with amiloride, the expressions of Matriptase, uPA, uPAR and MMP-2 mRNAs were detected by semi-quantitative reverse transcription polymerase chain reaction (RT-PCR) in human cervical cancer cell Hela.

**Results:** There were high expression of Matriptase, uPA, uPAR and MMP-2 mRNAs in Hela cell. After 24 hours incubation with different concentrations of Amiloride, 50µmol/L of Amiloride could cause the significantly decrease of the expressions of uPA, MMP-2 mRNAs in dose-dependent manner compared with the control group (P< 0.05), while it do not affect on the expressions of Matriptase and uPAR mRNAs (P>0.05). Treated with 150µmol/L Amiloride, the expression of uPA mRNA decreased obviously from 2 hours after treatment (P< 0.01), and the expression of MMP-2 mRNA decreased obviously from 4 hours after treatment (P< 0.05). There was obvious time-dependent manner between Amiloride and uPA, MMP-2 mRNA.

**Conclusions:** The low concentration of Amiloride could specifically inhibit the expression of uPA mRNA of human cervical carcinoma Hela cell lines in a concentration - time dependence, what could cause decrease of the expression of MMP-2 mRNA which was the uPA system's downstream factor, but do no effect to uPAR and Matriptase which was the uPA system's upstream regulator.
Poster Session II

THE EFFECT OF THE AMILORIDE ON MIGRATION AND INVASIVE ABILITY OF HUMAN CERVICAL CANCER CELL HEla IN VITRO

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Objective: To investigate the effects of Amiloride, which is the synthetic inhibitor of urokinase plasminogen activator, on the invasion, metastasis and apoptosis of Human Cervical Cancer Cell in vitro.

Methods: The cervical cancer cells Hela in logarithmic phase growth cells were randomly divided into the following groups as 5 ×10⁵ cells/ml density: control group, Amiloride 50 μmol/L, 100 μmol/L and 150 μmol/L group. At the treated with different concentration of amiloride 6, 12 and 24 hours, the migration ability of the cells was respectively detected by scarification assay and invasive ability by millicell chamber artificial reconstituted basement membrane invasion assay. Further, the cellular apoptosis was also analyzed by flow cytology.

Results: The 6,12,24 hour’ migration distance of Hela cells after 50,100,150μmol/L Amiloride incubation were significantly lower than the control group (all P< 0.01),and marked difference was also found between the 50, 100, 150μmol/L Amiloride groups (all P< 0.05).The number of Hela cells that penetrated the Matrigel after 50,100,150μmol/L Amiloride incubation decreased obviously in comparison with control group (F=226.95,P< 0.01); and marked difference was also found between the 50, 100,150μmol/L Amiloride groups (all P< 0.05).

Conclusions: Amiloride could decrease the invasion and migration ability of Hela cells in vitro in a dose-time-dependent pattern. Blocking the expression of the uPA mRNA expression may be a potential target for inhibiting cervical cancer metastasis.
Poster Session II

3D BASED ADAPTIVE BRACHYTHERAPY IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER IMPLEMENTATION OF GYN-GERSTROS GUIDELINES, EXPERIENCE AND CLINICAL RESULTS

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Purpose: To evaluate the treatment results of 3D based individually planned brachytherapy replacing standardized library plans for patients with locally advanced cervical cancer.

Methods: 63 patients, treated with curative intent in the period 2005-2010, received individually planned brachytherapy with applicator in situ. Each patient received 4 fractions, in combination with external radiation and weekly cisplatin. The treatment plans for the first 20 patients were based on CT, the rest on MRI. The patients were evaluated with regard to treatment response, recurrence, side effects and radiation damage for a period of at least 2 years.

Results: None of the patients experienced serious complications during the treatment. Except minor adjustments, all patients completed the treatment as planned. The doses to organs at risk were within the recommendations given by ESTRO. In contrast, when applying library plans these dose limits were exceeded for several patients. The target coverage was good; increasing when using MRI based planning compared to CT. So far 6 patients with serious late effects are observed. 2 patients did not have regression of tumour, 2 patients have recurred within the irradiated area, 9 patients recurred outside the radiation field and 9 patients are dead of disease.

Conclusion: Individually planned brachytherapy gives a better dose coverage to tumour and better control of doses to organs at risk than brachytherapy based on standardized library plans. The treatment is well tolerated and treatment results are good. We intend to follow our patient group further ~10 years focusing on serious late effect.
Poster Session II

OUTCOME OF CERVICAL CANCER TREATED WITH RADICAL HYSTERECTOMY IN ELDERLY PATIENTS


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Background and aim: Radical hysterectomy and pelvic lymphadenectomy (RHPL) is the infrequent procedure in treated elderly patients with early stage cervical cancer due to awareness of morbidity and uncertain result. To evaluate the outcome of this procedure in these patients, we conducted the comparative study to compare the outcome of cervical cancer treated with radical hysterectomy in patients aged more than and less than 60 years old.

Materials and methods: The data from medical record of 42 cervical cancer patients aged equal to or more than 60 years old were compared to 896 cervical cancer patients whose aged less than 60. All studied patients undergoing RHPL at Chiang Mai university hospital between January 2002 and December 2009. The basic data, the outcome and the morbidity in 2 groups were compared.

Results: The basic data of both groups were not significant difference in term of stage, previous conization , positive node, positive parametrium, positive surgical margin and adjuvant treatment. Elderly patients found adenocarcinoma less common than the younger group (4.8% vs. 22.4%, P=0.02). About the morbidity, both groups revealed similar complication rate (34.5% vs. 35.7%, P=0.53). The elderly patients and the younger patients developed recurrence 5.4% and 8.6%, respectively. The 5-year disease free survival of both groups were not significant difference (99.8% in elderly group vs. 89.7% in younger group).

Conclusion: Elderly cervical cancer patients revealed good outcome comparable to the younger age.
Poster Session II

RADICAL ABDOMINAL TRACELECTOMY IN TREATMENT OF INVASIVE CERVICAL CANCER PATIENTS

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Aim: To improve the surgical treatment of invasive cervical cancer (CC) directed at improving social rehabilitation of patients.

Materials: Radical abdominal tracelectomy (RAT) was performed in 40 CC patients with T1b1 stage, from 23 to 30 years (mean age 27.7±3.4). RAT included pelvic lymph dissection, abdominal extirpation of cervix uteri, proximal parametrectomy with intraoperative urgent histology of lymph nodes, cervix uteri and formation of uterovaginal anastomosis.

Results: Squamous cell carcinoma was histologically confirmed in all patients. In 32 patients electrocauterizing conization was performed before operation. The criterions of efficiency of RAT were: absence of cancer progression, renewal of menstruation, capability to child-bearing. In one case carcinoma with infiltrative growth in cut of proximal part of cervix uteri was detected under urgent hystology. Piver hysterectomy of III type was performed in this case. 5 patients had complications after operation such as the occurrence of pelvic lymphocysts which regressed after conservative treatment. The experience of RAT is positive: time of operation decreased to 130 ± 15 min, the volume of hemorrhage was less (270±50 ml) compared to Piver hysterectomy of III type. The mean quantity of days in hospital was 9,0±1,2. We didn’t detect recurrence of disease during 72 months.

Conclusion:

RAT indicates about possible its application in treatment of CC patients in reproductive age with T1b1 stage.

RAT allows preserving the reproductive and menstrual function in women in reproductive age.

RAT can be alternative method of treatment of patients with early stage of CC with preservation of reproductive function.
IDENTIFICATION OF NOVEL THIADIAZOLE DERIVATIVES THAT CAN INHIBIT PROLIFERATION AND INDUCE APOPTOSIS BY MODULATING NF-κB ACTIVATION IN CERVICAL CANCER CELLS

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Introduction: Constitutive activation of proinflammatory transcription factor NF-κB is frequently encountered in cervical cancer and regulates the expression of over 400 genes involved in proliferation, survival, metastasis and angiogenesis.

Objective: Thus NF-κB’s ability to control multiple genes involved in tumorigenesis makes it an attractive target for therapeutic development and novel agents that can interrupt NF-κB activation have enormous potential for the treatment of cervical cancer. Based upon the urgent needs for new lead compounds for cervical cancer therapy, we have synthesized a novel series of 4, 6-substituted 1,2,4-triazolo[3,4-b][1,3,4]thiadiazole derivatives and investigated their potential ability to modulate NF-κB activation.

Results: Four of the synthesized compounds, inhibited the proliferation of tumor cells and one derivative 5-(3-(2,3-dichlorophenyl)-1,2,4-triazolo[3,4-b][1,3,4]thiadiazol-6-yl)-2-flurobenzonitrile (SR6) suppressed invasion, induced apoptosis, and abolished the NF-κB activation in cervical cancer cells. Molecular docking analysis revealed that SR6 forms a number of interactions with the Arg33, Arg35, Tyr36, Glu39, Ser42, Ala43, and Gly44 residues involved in the binding of p50 domain with the p65 subunit and can alkylate the cysteine residue (Cys 38) in the DNA binding loop, after forming a H-bond with Arg35. Moreover, SR6 was found to decrease the expression of NF-κB regulated gene products, including those involved in proliferation, survival, invasion, angiogenesis and also suppressed the in vivo binding of NF-κB to the COX-2 promoter.

Conclusion: Overall our results suggest for the first time that thiadiazole derivatives have an enormous potential to be developed as novel NF-κB blockers for the treatment of cervical cancer.
Poster Session II

PREVALENCE AND TYPE DISTRIBUTION OF HUMAN PAPILLOMAVIRUS (HPV) IN NEW ZEALAND WOMEN WITH INVASIVE CERVICAL CANCER

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Background and aims: The epidemiology of HPV in New Zealand (NZ) women with invasive cervical cancer (ICC) is poorly documented. Maori women have a higher incidence and mortality from cervical cancer. This cross-sectional study aimed to document the HPV type distribution in NZ women with ICC. (StudyID: 111050).

Methods: Women with ICC diagnosed between 2004 and 2010 were identified from all NZ hospitals regularly treating cervical cancer. Women aged ≥18 years with ICC ≥stage IB were included in the study where consent could be obtained. Stored paraffin embedded cervical specimens were reviewed to confirm the diagnosis and test for HPV. A standardized HPV SPF10v1 PCR/DNA Enzyme Immuno Assay and the SPF10 v1 reverse hybridization assay were utilized.

Results: Cervical samples from 227 confirmed ICC cases were analyzed: 159 squamous cell carcinoma (SCC) and 68 adenocarcinoma (ADC) or adenosquamous carcinoma (ASC). HPV was detected in 88.5% of patients. The most common types detected were HPV-16 (51.1%), HPV-18 (20.7%), HPV-31 (4%), HPV-45 and -52 (3.1% each). Age, ethnicity, and cancer stage were not associated with the presence of HPV infection. Among HPV-positive patients, those ≥stage II were less likely to be infected with HPV-18 than the other types (p=0.029). Women identified as Maori tended to be younger and have higher stage disease than non-Maori. However no significant differences between these groups were seen.

Conclusion: HPV prevalence in NZ women with ICC is comparable to similar studies from other nations. Only minor variation of non-16/18 prevalence was identified between Maori and non-Maori women.
Poster Session II

BLEEDING AFTER LARGE LOOP EXCISION OF THE TRANSFORMATION ZONE (LLETZ): IS INFECTION OF THE UTERINE CERVIX A RISK FACTOR?

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Background and aims: The aim of this prospective study was to evaluate whether bleeding after large loop excision of the transformation zone (LLETZ) of the uterine cervix is influenced by genital pathogens.

Methods: The study included 1419 patients who underwent LLETZ for cervical intraepithelial neoplasia (CIN). Microbiological cervical smears were collected before the surgery. Postoperatively, the patients were observed for the occurrence of bleeding requiring secondary intervention.

Results: Cervical microbiology revealed genital pathogens in 714 (50.3%) patients and the absence of pathogens in 705 (49.7%) patients. The commonest groups of bacteria were group B β-haemolytic Streptococci, α-haemolytic Streptococci, Enterococcus sp. and coliforms. Secondary procedure because of severe bleeding was performed in 48 (6.8%) patients without and in 63 (8.8%) patients with genital pathogens, the difference was not statistically significant (chi-square = 1.72; P > 0.05).

Conclusion: Patients with CIN frequently harbour genital pathogens, which is not important for the occurrence of postoperative bleeding requiring secondary intervention after LLETZ.
Poster Session II

THE VALIDITY OF CONVERTING RADICAL HISTERECTOMY WITH THE INTRAOPERATIVE FINDINGS

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Objectives: In our institution, radical hysterectomy (RAH) for stage Ib to IIb cervical cancer is abandoned if the disease advances than expected such as para-aortic lymph nodes metastasis or abdominal dissemination, or if the procedure cannot be carried out because of the adhesion of the rectum or urinary bladder to the uterus. In such case, the surgery is quitted and converted to probe laparotomy or histerectomy. Subsequently, the patient receives radiotherapy and/or chemotherapy. The aim of this study is to estimate the validity of converting RAH according to the intraoperative findings.

Materials and Methods: We retrospectively analyzed the RAH abandoned patients in our institution from 2001 to 2010, and compared the prognosis with RAH completed patients. Moreover, in the abandoned patients, we compared the prognosis and recurrent pattern between RAH abandoned with advanced disease and the patients with unresectable disease.

Results: In 223 patients who had planned to perform RAH, 26 patients (11.6 %) were abandoned. The overall and progression free survival of the abandoned patients were significantly worse than that of the RAH completed patients. In 26 abandoned cases, 15 cases were abandoned with advanced disease, and 11 cases were with unresectable condition. Almost of all the patients with advanced disease had died of cancer with early distant metastasis. The local recurrence rate of the patients with unresectable disease was not inferior to that of RAH completed patients.

Conclusion: It is suggested that the surgery should be abandoned when the disease is advanced or technically impossible to complete it.
Poster Session II

A NEW POTENTIAL APPROACH FOR CERVICAL NEOPLASIA RISK ASSESSMENT IN HPV POSITIVE WOMEN

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A high MUC1 mucin expression is observed in metaplastic squamous epithelium of transitional zone in patients with cervical intraepithelial neoplasia. Objective of the study was to evaluate the MUC1 expression in cervical epithelium cells in women having nonneoplastic cervical disorders and urogenital infections.

Study group included 85 women (age median 31 years). Women were subjected to gynecological clinical evaluation, cervical Pap test, cervical DNA testing for HPV, and examination of MUC1 expression in cervical smears using immunofluorescence technique.

MUC1-positive metaplastic depolarized parabasal type cells (MUC1+ DP cells) in cervical smears were revealed in 18.5% cases in patients having endocervicosis, in 27% cases in patients having cervicitis or colpitis, in 40% cases in patients having cervical polyp.

MUC1+ DP cells in cervical smears were revealed in 43% cases in high-risk HPV positive patients, in 9% cases in HPV-negative patients and were not observed in any of 8 cases in low-risk HPV-positive patients.

In HPV16 and HPV18 positive patients MUC1+ DBP cells in cervical smears were revealed in 56% cases. Cytopathic virus-associated effects in MUC1+ cells was observed in HPV16 and HPV18 cases only.

The detection of MUC1+ DBP cells in cervical smears correlated with infection of M.hominis. In 63% of M.hominis positive cases co-infection of mycoplasma and high-risk HPV was observed.

Thus, the presence of MUC1+ DBP cells in cervical smears in women with nonneoplastic cervical disorders correlates to the most aggressive HPV types and, a predisposition to developing of cervical intraepithelial neoplasia in high-risk HPV positive.
Poster Session II

EFFECT OF AGE ON SURVIVALS OF CERVICAL CANCER PATIENTS WITH BONE METASTASIS

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Objective: To determine survivals of cervical cancer patients with bone metastasis relating with effect of age at the time of cervical cancer diagnosis.

Design: A retrospective analytic study.

Setting: Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

Sample: During January 1998 to December 2010, a total of 68 cervical cancer patients with bone metastasis were treated at Ramathibodi hospital.

Methods: Fifty-two medical records were identified and collected, the remaining sixteen medical records were not found.

Main outcome measures: Patient characteristics, clinical information, duration from cervical cancer diagnosis to bone metastasis diagnosis, survival time after bone metastasis and overall survival time.

Results: Among fifty-two cervical cancer patients with bone metastasis, there were 32 patients who were less than 55 years old, and 20 patients were 55 years old or more at the time of cervical cancer diagnosis. The elder group had less median overall survival than the younger group with statistically significant difference ($p<0.05$). However, there were comparable in the duration from cervical cancer diagnosis to bone metastasis diagnosis and the survival time after bone metastasis.

Conclusions: Elder patients with bone metastasis aged 55 years old or more at the time of cervical cancer diagnosis had poorer prognosis than the younger. To improve survivals and quality of life, more intensive treatments at the time of cervical cancer diagnosis in elder patients who could tolerate the side effects should be considered.
**Poster Session II**

**IMPROVED DETECTION OF HIGH-GRADE CIN USING A HAND HELD ELECTRICAL SPECTROSCOPY DEVICE**

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**Objective:** To determine if an Electrical Impedance Spectroscopy (EIS) device (APX100), as an adjunct to colposcopy, improves performance.

**Methods:** 474 women with abnormal cytology were enrolled. In phase one by comparing measured EIS spectra with ‘finite element models’ of cervical tissues, it was possible to derive a probability index for the presence of HG-CIN and a cut-off value for the detection of HG-CIN was derived for use in phase two. EIS data collection and analyses were performed in real time but the clinician was blinded to the EIS reading. All examinations were video recorded for analysis of performance.

**Results:** 214 were eligible in phase one and 215 in phase two. Average age 33·2 (median age 30·3; range 20-64) and 48·5% (208/429) had high grade cytology. In phase two, EIS increased the positive predictive value (PPV) to detect HG-CIN from 53·5% to 67% and specificity increased from 38·5% to 65·1%. If specificity is set as for colposcopic performance sensitivity increased to 96%. Analysis of the receiver operator characteristic (ROC) to detect HG-CIN showed that the area under the curve (AUC) was 0·887, an increase on clinical performance alone (p=0·02).

**Conclusions:** The study demonstrated the safety of APX100. Performance of APX100 is independent of the application of acetic acid. Using APX100, as an adjunct, PPV to predict HSIL can exceed 95%. APX100 is a clinically useful device for the detection of or absence of HSIL. It could prevent over treatment when using a 'see and treat' management strategy and enhance patient care.
Poster Session II

CERVICAL ENDOMETRIOSIS MIMICKING CERVICAL CANCER: A CASE REPORT AND REVIEW OF THE LITERATURE

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Introduction: We report a case of cervical endometriosis, which presented with symptoms and signs suspicious for a cervical malignancy.

Case: A 46-year-old woman presented to our institution with abnormal uterine and postcoital bleeding. On family history, her mother and aunt had endometrial cancer. On pelvic examination a 2 cm fragile endocervical mass was discovered. Also, a 3 cm partially firm mass was palpated originating from the posterior cervix. On transvaginal ultrasound a 3.5 cm semisolid mass originating from the posterior cervix was reported. She had high grade squamous intraepithelial lesion reported on pap-smear. CIN-III with positive margins was reported on loop electrosurgical excision procedure specimen. The fragile mass was reported as an infected endocervical polyp. Endometrial biopsy was reported as proliferative endometrium. Endocervical curettage was normal. She had elevated levels of CA125 (120U/ml), CA19-9 (51U/ml). Due to inaccessibility of the cervical mass, an exploratory laparotomy was planned. The patient desired no future fertility, and informed consent was obtained for hysterectomy for treatment of CIN-III. Upon exploration, a 3 cm cystic mass filled with chocolate brown fluid was discovered in the posterior cul-de-sac between the uterosacral ligaments. Hysterectomy was performed. Frozen section failed to report any malignancy and the operation was concluded. Final histopathology was reported as cervical endometriosis and CIN-III.

Discussion: Endometriosis is a very common disorder in reproductive age women. Although it generally presents with typical symptoms such as chronic pelvic pain or dysmenorrhea, rare clinical occurrences are not uncommon.
Poster Session II

HEAT SHOCK PROTEIN 27 AND P16 IMMUNOHISTOCHEMISTRY IN CERVICAL INTRAEPITHELIAL NEOPLASIA AND SQUAMOUS CELL CARCINOMA

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Heat shock protein 27 (hsp27) is expressed by squamous cell carcinoma of the uterine cervix and we have reported that hsp27 may be a diagnostic marker for cervical intraepithelial neoplasia (CIN) and carcinoma. P16 expression is also elevated in intraepithelial uterine cervical cancer and CIN2 or CIN3 lesions. However, it has been reported that p16 is negative in 5% to 20% of cervical cancer and CIN lesions. The present study was performed to immunohistochemically confirm the expression of hsp27 and p16 in cervical lesions. Formalin-fixed, paraffin-embedded cervical tissue specimens obtained between 2002 and 2010 were investigated for hsp27 and p16. We found positive staining for hsp27 in 63% of normal cervical tissues, 47% of CIN1 lesions, 75% of CIN2 lesions, 92% of CIN3 lesions, and 100% of squamous cell carcinomas (SCC). The corresponding rates for p16 positivity were 29%, 47%, 67%, 92%, and 75%, respectively. Positive staining for both hsp27 and p16 was observed in 6% of normal cervical tissues and in 19% of CIN1, 18% of CIN2, 85% of CIN3, and 75% of SCC specimens.

For identification of CIN3 or SCC lesions, hsp27 or p16 positivity had a sensitivity of 95.6% or 84.7% and a specificity of 37.2% or 70.5%, respectively. When both hsp27 and p16 were assessed, a sensitivity of 80.4% and a specificity of 87.0%, specificity was improved. In conclusion, both hsp27 and p16 immunohistochemistry is useful for the diagnosis of CIN3 lesions or cervical SCC.
**Poster Session II**

**ASSESSMENT OF THE PERFORMANCE OF THE DYNAMIC SPECTRAL IMAGING SYSTEM (DYSIS) IN THREE DIFFERENT CONCENTRATIONS OF ACETIC ACID SOLUTION**

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**Introduction:** We investigated the effect of three concentrations of acetic-acid solution on cervical acetowhitening and assessed the performance of DySIS in identifying high-grade disease.

**Methods:** DySIS is a novel digital colposcope, intended to assist colposcopists in identifying cervical neoplasia in-vivo, by quantifying and mapping the degree and duration of acetowhitenng during a three-minute period. We investigated the effect of three different acetic-acid concentrations in the diagnostic performance of DySIS. We enrolled 57 women with abnormal cytology. Each subject was examined with DySIS in three successive examinations (with at least 45 minute intervals), using 3%, 4% and 5% acetic acid, totaling 162 colposcopic examinations. All biopsies were submitted for histological assessment.

**Results:** The performance of the DySIS mapping in identifying in-vivo, high-grade cervical neoplasia was: a) sensitivity for 3%, 86%; for 4%, 79%; for 5%, 82% and b) specificity for 3%, 81%; for 4%, 77%; and for 5%, 77%. DySIS demonstrates very good performance in all concentrations, while the 3% shows the best performance. It was observed that morphological characteristics were better highlighted when using 5% acetic-acid.

**Conclusion:** We quantified for the first time the effect of the acetic-acid solution in the diagnostic information of the acetowhitenng and assessed the performance of DySIS mapping with three different concentrations of acetic-acid. DySIS demonstrated reproducibility, indicating that it can be operated with different concentrations with similar and high, performance. The fact that DySIS exceeded the typical colposcopic sensitivity suggests that it can assist the improvement of colposcopic performance in detecting and grading, cervical neoplasia in-vivo.
Poster Session II

ABSENCE OF DYSPLASIA IN THE EXCISED CERVIX BY A LOOP OR LASER CONE PROCEDURE IN THE TREATMENT OF CIN


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Objective: Absence of dysplasia in the excised specimen following Loop or Laser excisional procedure for treatment of cervical intraepithelial neoplasia (CIN 1/2/3) is an occasional finding of uncertain clinical significance. We analyzed the incidence of negative cone biopsies and evaluated the significance of the findings.

Materials and methods: The study population consisted of women who underwent cervical conization at a university teaching hospital during 2011. In total 299 women (mean age 39.8 +/- 10.2 years) with biopsy proven CIN 1/2/3 or due to cytology/histology discrepancy were treated by Loop or Laser conization. Negative cone biopsies were defined as those not showing evidence of HPV, CIN or invasive disease.

We evaluated several factors including age, method of excision, volume of the excised cervix and also referral cytology, histology of the women with negative cone biopsies.

Results: During this study period 299 conizations were performed. Of these 20 (6.8%) were negative. 65% of those women were over 45 years of age and this group of women had mean age (50.7 +/- 9.9 years) in contrast with the LSIL group (39.6 +/- 9.7 ) or the HISL group (38.4 +/- 9.9 ), p < 0.001. The mean maximum cone diameter 1.7 +/- 0.6 cm was significant smaller (p=0.009) than the diameters in LSIL and HSIL. Furthermore mean maximum cone depth was 0.6 +/- 0.4 cm, significant smaller than the mean depth in LSIL or HSIL, difference statistically significant (p< 0.001).

29.4% of the women with negative cone biopsies had referral cytology negative, 35.3% ASCUS, 11.8% LSIL and 23.5% HSIL. 14.3% had a biopsy showing HPV, 64.3% CIN1, 14.3% CIN2 and 7.1% CIN3.

Conclusion: Even there is no dysplasia in conization specimens, close follow is needed.
Poster Session II

CERVICAL CYTOLOGY/CONE BIOPSY HISTOLOGY DISCREPANCY: A YEAR REVIEW


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Objective: To determine the concordance between cervical cytology and cone biopsy histology in women who underwent cervical conization at a university teaching hospital from January 2011 to December 2011.

Materials and methods: During the study period, 299 conizations were performed for treatment of CIN or due to cytology/histology discrepancy. Cervical samples were taken using a Cervex Brush and Ayre Spatula collection device from patients referred to the colposcopy clinic. A conventional smear was prepared on 2 glass slides. An experienced cytopathologist whose diagnostic experience exceeds 20 years and a senior cytotechnologist examined all samples. All cone specimens were examined from 2 experienced pathologists skilled in gynaecological pathology.

Results: Referral cytology was negative in 11.2% of women, ASCUS in 13.45, LSIL in 41.7%, CIN2 in 14.9%, CIN3 in 15.95 and microinvasion or invasion in 2.9%. Cone specimen histology was negative in 6.8%, HPV 10.8%, 43.1% CIN1, 17.3% CIN2, 17.6% CIN3 and 4.4% invasive disease. The concordance rate between referral cytology and cone specimen histology was for the categories negative, HPV, CIN1, CIN2, CIN3 and cancer 58.2%. The concordance rate was 74.6% in the correlation between low grade and high grade disease. Furthermore referral cytology demonstrated a sensitivity 60.4%, specificity 85.7%, positive predictive value 74.7% and negative predictive value 75.8% for prediction of high grade intraepithelial neoplasia as determined from cone specimen histology.

Conclusions: The agreement between cervical cytology and cone specimen histology, considering the CIN grade, was moderate. Ideally, all cases with discrepancy in high-grade cytology, colposcopy and histologic lesions should be discussed in a multidisciplinary meeting.
Poster Session II

PREDICTORS AND CLINICAL SIGNIFICANCE OF THE POSITIVE CONE MARGINS IN CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) PATIENTS


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Objective: To identify the factors associated with positive margins of conization, in patients with CIN.

Materials and methods: Analysis of 299 patients aged 39.8 years (SD=10.2 years) with CIN who underwent conization (Loop or Laser), from 1 January 2011 to 31 December 2011, evaluated in terms of referral cytology, preoperative histology, cone biopsy histology, number of specimens excised, thermal artefacts and correlated with positive cone margins.

Results: Endocervical, ectocervical and both endocervical and ectocervical positive margins were identified in 24 (9.9%), 10 (4.1%) and 12 patients (5%), respectively.

HGSIL in either cytology or preoperative histology, was significantly correlated with positive cone margins. Positive cone margins was found more frequently in HGSIL, than LGSIL, ASCUS or negative cytology (35% versus 10.7%, p<0.001).

The frequency of positive margins was notified to be higher when the preoperative histology was high grade in contradiction with low grade histology (24.5% versus 11.8%, p=0.017).

Furthermore positive margins were identified more frequently in patients who underwent Laser (50%), versus combined Loop-Laser (33.3%) or Loop conization (17.7%), p=0.042.

We additionally demonstrated that the frequency of positive cone margins was higher in patients who underwent conization in multiple, than in two or in one specimens (36.1% vs 20.7% vs 10.5%, p=0.003).

Finally the frequency of positive cone margins was higher in cases of thermal artefacts, (100% vs 18.3%, p=0.035).

Conclusions: Our results suggest that positive margins/residual CIN may be a valuable surrogate marker for further clinical management of CIN. Choice between additional surgery or follow-up in the young patients with positive margins who want to preserve their fertility depends on the grade of the lesion.
Poster Session II

PELVIC EXENTERATION FOR GYNECOLOGIC MALIGNANCIES

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The objectives for pelvic exenteration are:

1. treatment of advanced gynecologic cancer
2. treatment of recurrence of gynecologic cancer
3. palliative treatment for advanced gynecologic cancer with extensive fecal and/or urinary fistulas or relieve of pain in such advanced cases.

First description of the pelvic exenteration surgery was made approximately 60 years ago by Bruschwig (1948) He described the four types of pelvic exenteration operations: anterior, posterior, complete/total and partial pelvic exenteration. A 5-year survival of 19%.

Modern postoperative care and reconstructive surgical possibilities (neo-bladder; low rectal anastomosis; neo-vagina) with multidisciplinary involvement has made a significant better morbidity, mortality (1.4%-4%) and a higher quality of life for patients treated with this radical exenterative procedures. 5-year survival rates of 30%-60% was achieved in many specialized centers.

- Between 1983 and 2010: 124 pelvic exenterations were performed in our institutions (Erlangen and Bayreuth); 93 because of advanced gynaecologic malignancies. Mean age of the patients is 54 years.
- All patients are followed, mean observation time 84 months.
- For advanced primary cervical cancer with extensive bladder and/or rectal invasion and/or extensive vaginal infiltration mean survival rate of more than 28% can still be achieved in our institution.
- After the follow up time 46% of the patients with pelvic exenteration are still alive.

Conclusion: Pelvic exenterations performed by multidisciplinary setting (gynaecologic oncology, surgery and urology) are being performed more frequently in many gynecologic cancer centers and with continious improvement of therapeutic results, morbidity and mortality as well as quality of life.
Poster Session II

SURGERY AFTER INTENSITY MODULATED ARC THERAPY IN THE TREATMENT OF LOCALLY ADVANCED CERVICAL CANCER: FEASIBILITY AND SURGICAL OUTCOME

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Introduction: Adding chemotherapy to radiotherapy has improved survival rates for locally advanced cervical cancer (LACC), although they are still disappointing. Therefore the idea of surgery post chemo-radiation was adopted. One of the concerns regarding post-chemoradiation surgery is surgery-related morbidity.

Aim: To investigate the feasibility of surgery after improved radiotherapy techniques such as Intensity Modulated Arc Therapy (IMAT) and to describe the associated morbidity.

Methods: Prospective study of primary inoperable LACC patients. All patients underwent IMAT, combined with weekly Cisplatin when possible. Thereafter, resectability was re-evaluated. If resectable, patients were treated with Wertheim type 2 surgery + pelvic lymphadenectomy (on PET-CT indication). If not resectable, patients were treated with brachytherapy.

Results: Since 2006, 41 consecutive patients were included. After neoadjuvant IMAT (± cisplatin), 34 were considered resectable and underwent surgery (brachytherapy: 5; progressive disease: 1; intercurrent death: 1). The mean operative time was 116 minutes. The mean estimated bloodloss was 500ml. No ureter, bladder or bowel injuries occurred. The operative mortality rate was nil. No postoperative urinary/digestive fistulae or stenosis were noted. Eleven patients had postoperative urinary retention problems. At the time of discharge, 5 patients needed self-catheterisation. All problems resolved within 3 months. In 4 cases we saw clinical significant lymphocele. In the Wertheim-group OS and DFS at 3 years are 81% and 91% respectively versus 63% and 74% for the whole study population.

Conclusions: Surgery for LACC is feasible and complication rates are comparable with those of primary surgery for cervical cancer.
Poster Session II

CLINICAL OUTCOME OF STAGE IA1 SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX AND PATHOLOGICAL FINDINGS OF INITIAL CONIZATION

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Aim: The present study investigated the clinical outcome of stage Ia1 squamous cell carcinoma (SCC) of the uterine cervix at a single institute.

Materials and methods: Subjects were 84 patients with cervical SCC, International Federation of Gynecology and Obstetrics stage Ia1 diagnosed according to conization findings between January 2000 and June 2009. Correlations between clinical outcome and pathological findings on initial conization were investigated.

Results: Of 65 hysterectomy (without pelvic lymphadenectomy) patients, two (3.1%) showed metastasis to the vaginal wall, and two (3.1%) to the pelvic lymph nodes. Five patients (6.0%) showed lymphovascular invasion, and three (3.6%) showed confluent patterns of stromal invasion (confluent invasion) on initial conization findings. All of these five patients were included in the hysterectomy group. Of 19 patients with conization alone, two showed vaginal metastasis. Of four patients with vaginal metastasis, two showed lymphovascular invasion and one showed confluent invasion despite negative conization margin. In patients with nodal metastasis, stromal invasion of 3.0 mm and 2.8 mm, and horizontal spread of 6.8 mm and 6.9 mm were observed on conization, respectively. All patients are currently alive due to adequate therapy including chemo-radiation for six patients with recurrent disease.

Conclusions: In patients showing stromal invasion of nearly 3.0 mm and horizontal spread of nearly 7.0 mm in stage Ia1 cervical SCC, pelvic lymphadenectomy may be considered. Even for patients showing a negative conization margin, careful follow up is necessary, because vaginal metastasis sometimes occurs.
Poster Session II

THE PI3K-AKT PATHWAY MAY BE INVOLVED IN CARCINOGENESIS OF UTERINE CERVICAL CLEAR CELL CARCINOMA

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Objective: Cervical clear cell carcinoma (CCCC) is a rare cervical neoplasm and is known to have little relationship with high-risk HPV. Our objective was to analyze clinical features, treatments, and prognosis, and to clarify activated signaling pathways of CCCC.

Methods: A retrospective review was conducted at Hyogo Cancer Center of all primary CCCC between 1988 and 2011. Tissues from the cases were immunostained for EGFR, HER2, phospho-AKT and PTEN.

Results: CCCC was confirmed in 13 patients. The median age was 67 years (range, 36-85 years). The FIGO stage was as follows: 6 patients (46%) were stage Ib, 4 (31%) were IIb, 2 (15%) were IIIb and 1 (8%) was IVb. The first symptom observed in all of the patients was abnormal genital bleeding. Pap smears were also abnormal in all of these patients. No recurrence was observed in any of the patients with stage Ib. Although only 2 out of 8 cases (25%) without pelvic node metastasis showed a recurrence, 4 out of 5 cases (80%) with pelvic node metastasis showed recurrence and died of the disease. In IHC, overexpression of EGFR (10/12), HER2 (8/12), and phospho-AKT (7/12), and loss of PTEN (6/12) was observed in CCCC.

Conclusion: Despite the good prognosis of stage 1 CCCC, cases with lymph nodes metastasis showed a poor prognosis. Our immunostaining results suggest that the PI3K-Akt pathway contributes to carcinogenesis of CCCC. This finding could lead to additional therapeutic options targeting a specific blockade of the PI3K-AKT pathway.
Poster Session II

PROGNOSTIC FACTORS FOR CERVICAL CANCER TREATED WITH RADICAL HYSSTERECTOMY AND SYSTEMATIC LYMPHADENECTOMY

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Objectives: The purpose of the present study was to identify prognostic factors in patients with stage IB-IIA cervical carcinoma who had undergone radical surgery including systematic lymphadenectomy.

Methods: 160 patients with stage IB to IIA cervical carcinomas were retrospectively analyzed. The median follow-up period was 95 months. Cox regression analysis was used to select independent prognostic factors.

Results: Lymph node status, parametrial invasion, lymph-vascular space invasion, and histology type adenocarcinoma were found to be independently related to patients' poor survival. For patients with a tumor histologically confined to the uterus and have neither parametrial invasion nor lymph node metastasis, LVSI was the most important prognostic factor. The survival of patients with a tumor extending to parametrium or pelvic lymph node(s) was adversely affected by histology of pure adenocarcinoma. Tumor extended to common iliac or paraaortic nodes, resulted into patients' poor survival. Patients' prognosis could be stratified into low risk (patients with a tumor confined to the uterus not associated with LVSI: n=72), intermediate risk (patients with a tumor confined to the uterus associated with positive LVSI, and patients with squamous/adenosquamous carcinoma associated with pelvic lymph node metastasis or parametrial invasion: n=76), and high risk (patients with pure adenocarcinoma associated with pelvic lymph node metastasis or parametrial invasion, and patients with common iliac/paraortic node metastasis: n=9).

Conclusions: LN status, parametrial invasion, LVSI, and histology of pure adenocarcinoma are important histopathologic prognostic factors of cervical carcinoma treated with radical hysterectomy and systematic retroperitoneal lymphadenectomy.
Poster Session II

INCIDENCE UNSATISFACTORY RATE CERVICAL CYTOLOGY CLASSIFICATION IN LIQUID-BASED VERSUS CONVENTIONAL CERVICAL CYTOLOGY

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Background and aim: The papanicolaou (pap) smear has been used to screen women for cervical cancer since 1940. Unsatisfactory results induce anxiety in patients and doctors. Recently, a number of new technologies have been developed to improve the detection of cervical cancer. Increase the early detection of meaningful pap smear abnormalities, reduce the number of unsatisfactory smears and false negative results and provide fewer ambiguous results one of these method is the new test, include liquid-based to improve the quality and quantity of the cervical pap smear. The aim of this study is to evaluate rate of unsatisfactory smear of cervical cytology in two methods, conventional pap smear (CP) and liquid-Based (L.B).

Methods: A comparison cross-sectional study was performed from 2004-2005 on 1500 patients referred to Ghaem hospital and private clinic. From all patients cervical cytology was taken randomly via two methods CP and L.B. Subsequently frequency unsatisfactory cervical cytology in tow methods evaluated. Statistical analysis using the SPSS soft ware was done and t-test and c2 used for comparative evaluation.

Results: Considering the incidence of unsatisfactory cervical cytology in CP method %0.3 was and in LB method %1 was. Sensitivity of the C.P method was 68.8% and that of the L.B method was 83.1%.

Conclusion: In this study incidence unsatisfactory rate in L.B method was higher than C.P method.
**Poster Session II**

**EVALUATION OF REIDS COMBINED COLPOSCOPIC INDEX AS A PREDICTOR OF CERVICAL INTRAEPITHELIAL LESION (CIN)**

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**Background:** Carcinoma cervix is commonest cancer among women worldwide. India - 11.3-38.9/lakh women, accounts for 80% of all genital cancers.

**Aims:** Prospectively to evaluate reid’s score prediction for CIN.

**Methods:** Colposcopy done in 125 patients with clinically suspicious cervix. Colposcopic directed cervical biopsies performed in keratotic lesions, colposcopically abnormal lesions and unsatisfactory findings. Endocervical curettage in unsatisfactory colposcopy.

**Results:** Patients were married, parous, non-pregnant. Abnormal Colposcopic Findings (n=62) showed Low grade disease (0-2) in 47 patients [CIN1 - 4, CIN 1 (HPV) - 2, Ch. Cervicitis - 34, Ch. Cervicitis with sq meta - 6, Ch cervicitis with ero - 1], Intermediate grade disease (3-4) in 11 [CIN 1 - 4, Ch. Cervicitis - 5, Ch. Cervicitis with meta - 2] and High grade disease (5-8) in 4 patients [Sq. cell ca. - 1, CIN 1 - 1, Ch. Cervicitis with endometrial adenoca. - 1, Ch. Cervicitis - 1].

Colposcopy of 1 patient suggested invasive carcinoma and histopathology confirmed microinvasive squamous cell carcinoma. Six patients with unsatisfactory colposcopy showed benign histopathology.

**Conclusions:** Overall predictive value of colposcopy for preinvasive and invasive disease was 20.63% with 79.73% false positive rate.

Sensitivity, specificity, predictive value and false negative rate of colposcopy for invasive disease was 50%, 100%, 100% and 1.61% respectively with 98.41% diagnostic accuracy.

Colposcopy distinguishes normal cervix from cervix with intraepithelial neoplastic lesions, avoids need of cone biopsy and associated morbidity. Patients with low grade disease, regular follow-ups recommended to see progression of lesion.
The role of p16INK4a in cervical intraepithelial neoplasia

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The aim of our study was to evaluate the expression of p16INK4a in women treated for cervical intraepithelial neoplasia (CIN). Between June 2010 and January 2012, we performed 62 consecutive loop electrical excision procedure (LEEP) at the Department of Gynecologic Oncology of Turin.

Cellular expression of p16 was evaluated through immunohistochemical methods on tissue samples obtained through LEEP. The mean age was 32 years and most of patients were nulliparae (59%) and did not smoke (70%). Pap smear was performed to each women: HSIL was found in 26 patients (42%), while LSIL in 32 cases (52%). Cervical punch biopsy resulted in slight and mild-severe dysplasia, respectively in 34% and 48% of patients. Histological analysis on tissue samples showed 25 cases of CIN 1 and 37 cases of CIN 2-3 (in two patients was also found CIS). Immunohistochemical detection of P16 demonstrated an over-expression in patients affected by CIN 2-3 (33 patients, 90%) and in 8 cases of CIN1 lesions (32%). Diffuse strong immunostaining for P16 was observed in 34 biopsies (85%) and mostly correlated with HSIL (>88%). No difference in severity of lesion between smokers and not smokers was observed in women with over-expression of P16.

The expression of P16 is known to be elevated in high degree CIN lesions suggestive of integrated high-risk HPV DNA into the host genome (3). However, some CIN1 lesions can over-express P16: a new study may be useful in its evaluation as a marker of the progression risk of low-grade cervical dysplasia.
A PROSPECTIVE CROSS-SECTIONAL STUDY OF QUALITY OF LIFE IN CERVICAL CANCER PATIENTS TREATED WITH RADIOTHERAPY

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Purpose: Increasing survival in patients treated for cervical cancer supports increasing importance of quality of life assessment (QOL). The goal of this study was to assess treatment related QOL in patients with cervical cancer (PCC) treated with radiotherapy (RT).

Methods and materials: This is a prospective IRB approved cross-sectional study of PCC treated with external beam radiotherapy (EBRT) +/- low dose rate (LDRB) or high dose rate (HDRB) brachytherapy, +/- surgery, +/- chemotherapy from 1998-2011. All patients completed the European Organization for the Research and Treatment of Cancer QLQ-C30, QLQ-CX24, and HADS/Rosenberg self-esteem test at time of study enrollment.

Results: Sixty PCC were enrolled, with FIGO Stage 1-2 (n=50), Stage 3-4 or recurrent (n=10). Treatment was as follows: surgery (n=15), chemotherapy (n=48), HDRB (n=39), LDRB (n=10). Median age at treatment completion was 50 years (range 24-77). Median follow-up at QOL completion was 2.7 years. Global Health Score (GHS) was 69 and 73 in patients the EBRT/Surgery and EBRT respectively (P=0.46), 75 and 65 in patients with and without chemotherapy respectively (P=0.03), 75 and 69 in patients with follow-up < 3 and >3 years respectively (P=0.21), 74 and 70 in patients treated with HDRB and LDRB respectively (P=0.46).

Conclusion: Patients treated with radiotherapy and surgery vs radiotherapy alone did not have a statistically significant different reported QOL. There was a statistically significant QOL difference in patients based on chemotherapy administration. There was no significant difference in QOL based on LDR or HDR brachytherapy.
Poster Session II

THE SURVIVAL ANALYSIS OF STAGES IIA1 AND IIA2 CERVICAL CANCER PATIENTS

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Background and aims: The goal of this paper is to assess the benefits of the 2009 FIGO staging system for the survival of patients with stages IIA1 and IIA2 cervical cancer (Cx Ca).

Methods: A study cohort of 51 patients with stage IIA Cx Ca were retrospectively collected from 2004-2009 hospital-based, long-form Cx Ca data registry at Mackay Memorial Hospital (Taipei, Taiwan). The survivorship and overall survival were compared between these two groups using log-rank test.

Results: Thirty-six and fifteen patients were classified into stages IIA1 and IIA2, respectively. Stage IIA2 patients were young than those with stage IIA1 disease (mean age, 47.4 vs 55.1 years, \( p=0.008 \)), but no significant difference was observed in confirmed LNp status (21.4% vs 38.5%, \( p=0.280 \)) between them. Although the 2- and 5-year overall survival was better among stage IIA1 patients, there was no significant difference in survival between stage IIA1 and IIA2 groups (2-year, 90.6% vs 77.8%; 5-year, 86.3% vs 51.9%, \( p=0.218 \)).

Conclusions: Although survival differences between IIA1 and IIA2 patients are not statistically significant, the revised FIGO 2009 staging system for Cx Ca defines a group of stage IIA patients with bulky tumor (stage IIA2) that are generally younger than stage IIA1 patients. It is sensible to investigate an alternate or enhanced treatment scheme for stage IIA2 patients. Ideally, the treatment scheme should prevent unnecessary radical surgery if a patient can be exposed to either chemotherapy, radiotherapy, alone or in combination.
HELA CELLS SUPPRESS NK CELL CYTOTOXICITY THROUGH UP-REGULATION OF SIALIDASE AND GD3


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Background and aims: Gangliosides and sialidases may regulate the interaction between tumor cells and immune cells through regulating NK cell activity in cervical cancer patients.

Methods: In order to test this hypothesis, NK cells were co-cultured with a cervical cancer cell line, HeLa cells, and clinical specimens, including normal cervical tissue and cervical cancers were also evaluated by immunohistochemical staining.

Results: High expression of GD3 and sialidase on HeLa cells could suppress NK cell cytotoxicity in co-culture conditions. The use of a sialidase inhibitor (DANA) could partially restore the suppressed cytotoxicity of NK cells in a co-culture condition. Western blot showed that sialidase involved this suppression effect on NK cells. The clinical significance of sialidase showed that sialidase was also overexpressed in the cervical cancer tissues, compared with the normal cervix.

Conclusion: We concluded that sialidase may play an important role in the interaction between the NK cells and cervical cancer.
Poster Session II

RADICAL TRACHELECTOMY FOR CERVICAL CANCER WITH TUMOR ≥2 CENTIMETERS: AN INTERNATIONAL SERIES OF 86 PATIENTS

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Objectives: As experience with abdominal radical trachelectomy increases, the relative contraindication of size ≥ 2cm is questioned. We report our trachelectomy experience with tumors ≥ 2cm, describing the oncologic outcomes.

Methods: An international collaboration at 2 institutions identified patients scheduled for radical abdominal or vaginal trachelectomy, 2001-2011. Largest tumor dimension was determined by physical exam, MRI, or pathology (cone/LEEP+trachelectomy). Clinical and demographic data were gathered.

Results: In all, 86 of 208 (37%) patients had tumors ≥2cm (2-4cm); 72 were documented by exam or MRI and 14 by pathology (cone/LEEP/trachelectomy or summation of tumor size on cone/LEEP/trachelectomy). Mean age was 30yrs (20-44). Sixty-four(74%) were nulliparous. In all, 80(93%) procedures were performed abdominally, the remainder vaginally. Fifty-eight(68%) had squamous carcinoma, 21(24%) adenocarcinoma, and 7(8%) adenosquamous. Median 24 (7-57) lymph nodes were removed. Eighteen(21%) patients had positive nodes. Eight(9%) had positive internal os margins. Due to intraoperative frozen-section, 17(20%) patients underwent immediate hysterectomy and 1(1%) definitive chemoradiation. Due to high-risk pathologic features, 30(35%) patients received chemoradiation.

In total, 53/86(62%) patients with tumor ≥2cm preserved fertility potential (no hysterectomy or chemoradiation). There are no recurrences, median 26month follow-up.

Conclusions: Expanding radical trachelectomy inclusion criteria to young women with ≥2cm tumors allows a fertility-sparing procedure in a significant proportion of cases who would otherwise be denied the option with no apparent compromise in oncologic outcome. Novel fertility-sparing options such as neoadjuvant chemotherapy and postoperative chemotherapy without radiation should be explored further to see if more cases could be managed safely without loss of fertility.
Poster Session II

THE EFFICACY OF NERVE SPARING TECHNIQUE DURING RADICAL HYSTERECTOMY IN REDUCING POST OPERATIVE URINARY RETENTION: EXPERIENCE IN JAKARTA, INDONESIA

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Objectives: To describe the efficacy of nerve sparing during radical hysterectomy technique and the impact it has made in our institution. We collected cervical cancer patients whom underwent radical hysterectomy with and without nerve sparing technique and observed differences in post operative urinary retention.

Methods: Thirty four patients with FIGO stage IB-IIA cervical cancer underwent radical hysterectomy and bilateral lymphadenectomy from January 2011 to December 2011. Postoperative assessment of urinary retention was

(a) post-void residual urine volume during initial bladder training,
(b) time to achieve post-void residual urine volume less than 100 ml, and
(c) presence of urinary retention.

Results: A total of fifteen patients underwent nerve sparing (NS) technique during radical hysterectomy. Isolation and preservation of hypogastric nerve, splangnic nerve and bladder branch of inferior hypogastric plexus was conducted in 70%, 50%, and 32.4% of the patients, respectively. No differences was found in post-void residual urine volume (Mean 247 ml (NS) VS 365 ml (Non NS), P >0.05), time to achieve residual urine volume less than 100 ml (Mean 23.3 days (NS) VS 18.4 days (Non NS), P >0.05) and presence of urinary retention (P>0.05).

Conclusion: Further evaluation and training are needed for better establishment in the role of nerve sparing technique in our institution. Several factors may explain our findings include inappropriate selection criteria of patients in nerve sparing group, insufficient training hours, and improper evaluation method. Much needs to be done to constitute better care and service for cervical cancer patients.
**Poster Session II**

**PROSPECTIVE EVALUATION OF THE ACCEPTABILITY AND COMPLIANCE WITH POSTPARTUM HUMAN PAPILLOMAVIRUS VACCINATION IN YOUNG WOMEN**

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**Background:** Despite the efficacy of vaccines against human papillomavirus (HPV), vaccination rates remain low in many countries. We examined the acceptability and satisfaction of HPV vaccination in postpartum women.

**Methods:** Postpartum women 18-26 years of age were offered the quadrivalent HPV vaccine. Women were vaccinated during hospitalization after delivery, at the 6-week postpartum visit, and at a third dedicated vaccination visit. The primary outcome was patient acceptability and satisfaction. Secondary outcomes included the influence of knowledge and attitudes of HPV, decisional conflict, and satisfaction on completion of all 3 vaccines.

**Results:** A total of 150 women were enrolled. Overall, 7 (4.7%) women did not receive any doses of the vaccine, 62 (41.3%) received 1 dose, 35 (23.3%) received 2 doses, and 46 (30.7%) completed the series and received all 3 doses of the vaccine. Knowledge of HPV, HPV-related disease, attitudes about HPV, and decisional conflict were not associated with completion of the vaccine series (p=NS). The vaccine was well tolerated with few side effects. The majority of women reported a high-degree of satisfaction with postpartum vaccination; 96.7% thought vaccination was worthwhile, 98.0% thought postpartum vaccination was convenient and 98.7% were happy they participated. Further, 50.1% of women reported that they would not have otherwise asked about vaccination. After vaccination, only 17.3% said they would have rather made a separate trip for vaccination.

**Conclusion:** A strategy of postpartum HPV vaccination is convenient and associated with a high-degree of patient satisfaction. Further interventions to improve completion of the series are needed.
Poster Session II

MIR-21 SUPPRESSES RADIOSENsitIVITY IN CERVICAL CANCER

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Purpose: To study the relation between miR-21 expression and radiosensitivity in cervical cancer, and to find the mechanism of miR-21 regulate the radiosensitivity of cervical cancer.

Methods and materials: Cervical cancer cell, SiHa and Me180, are transfected by miR-21-mimic, miR-21-inhibitor. Colony-Formation Assay was performed to detect the radiosensitivity. With agomir-21, and agomir-NC in vivo experiments to verify the radiation sensitivity of stably transfected lines. Through cell proliferation assay, cell cycle assay and apoptosis assay, we searched for the molecular mechanism which miR-21 depressed radiosensitivity. Furthermore, three prediction algorithms PicTar, TargetScan and DianaLab were used to analyze the possible target gene.

Results: The overexpression of miR-21 can inhibit the radiosensitivity of cervical cancer cell, while low expression of miR-21 can promote the radiosensitivity of cervical cancer cells. We use the expression of miR-21 angomir injected into nude mice tumors, showing miR-21 can inhibit the radiosensitivity of cervical cancer in vivo. Furthermore, miR-21 can promote cell proliferation, inhibit apoptosis, and does not affect the cycle distribution. Except for proliferation, cell cycle, apoptosis experiments, we also use bioinformatics software to predict the target gene of miR-21, YAP-1 becomes the candidate.

Conclusions: We conclude that miR-21 regulates radiosensitivity in cervical cancer through regulating apoptosis.
Poster Session II

CANCER OF THE CERVIX IN UNSCREENED WOMEN

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Background: Cancer of the cervix remains an important health problem amongst women worldwide. Widespread comprehensive cervical cancer control programme have resulted in marked reduction in incidence and mortality in most developed countries. Developing countries bear over 80% of the global burden, with only 5% of global resources for cancer control. Majority of the cases in these countries present late and are incurable at the time of diagnosis.

Aim: To review the presentation and histopathological types of cervical cancer cases seen in Aminu Kano Teaching Hospital Kano, over sixteen year period(1995- 2010).

Material and methods: Case records of histopathologically diagnosed cancer of the cervix were retrieved. Demographic data stage of the tumor at presentation and histopathologic type was extracted. The results were analysed using descriptive statistics.

Results: Six-hundred and sixty gynaecological cancers were seen during the study period, cancer of the cervix accounting for 386(58.5%). Majority of the patients (71.1%) were grand-multiparous and majority (91.8%) presented with advanced disease. Squamous cell carcinoma accounted for 86.3% of the cancers, adenocarcinoma 12.4%, others 1.3%.

Conclusion: Cancer of the cervix is the commonest gynaecological cancer at Aminu Kano Teaching Hospital, Kano, Nigeria. Squamous cell carcinoma is the commonest histological type.
**Poster Session II**

THE ROLE OF ELECTIVE PARA-AORTIC LYMPH NODE IRRADIATION IN PELVIC LYMPH NODE POSITIVE CERVIX CANCER PATIENTS RECEIVING CONCURRENT CHEMO-RADIATION

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**Objective:** The benefit of elective para-aortic lymph node irradiation (PART) for cervix cancer is unclear in the setting of concurrent cisplatin chemotherapy administration. We compared the outcomes of cervix cancer patients with pelvic lymph node positive disease treated with pelvic RT (PRT) with or without PART.

**Methods:** Patients treated with chemo-radiotherapy for pelvic node positive, non-metastatic cervix cancer between 1999-2010 were identified in a prospective database. The treatment involved external beam radiotherapy to the pelvis delivered concurrently with weekly cisplatin chemotherapy, followed by pulsed dose-rate intracavitary brachytherapy. Patients with PART received radiotherapy to the paraaortic chain or 'mini'-PART (mPART) to lower paraaortics only. Survival outcomes were analysed using Kaplan-Meier and log-rank tests. Paraaortic relapse rate and late toxicities were analyzed using a competing risk method.

**Results:** There were 67 patients identified with a median follow-up time of 3.6 years. The addition of PART (n=46) did not result in improvement in DFS compared to those treated with PRT (n=21), 38% vs 42%(p=NS). Similarly, there was no difference in 3Y OS (62% vs 63%, p=NS). Six patients (9%) developed isolated paraaortic recurrences, three received PRT and 2 received mPART and relapsed out of field. Patients receiving PART had a trend towards higher grade 3/4 late toxicity than those who received PRT, 10.9% vs 0% (p=0.12).

**Conclusion:** These results suggest that the addition of PART for pelvic node positive cervix cancer patients treated with concurrent chemo-radiotherapy does not improve survival. The potentially higher rate of late toxicity should be considered.
Poster Session II

SURVIVAL AND SURGICAL OUTCOMES OF ROBOTIC RADICAL HYSTERECTOMY USING 3 ROBOTIC ARMS COMPARED WITH ABDOMINAL APPROACH FOR CERVICAL CANCER

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Purpose: To compare surgical outcomes and survival rates of robotic radical hysterectomy (RRH) and abdominal radical hysterectomy (ARH) in the treatment of early-stage cervical cancer.

Methods: One hundred fifty six consecutive patients with FIGO stage 1A2 to IIB cervical cancer who underwent RRH (n=78) or ARH (n=78) between June 2006 and December 2011 were evaluated. Radical or modified radical hysterectomy with pelvic lymphadenectomy was performed in all patients.

Results: All RRHs were completed robotically with no conversions to laparotomy. RRH showed favorable outcomes over ARH in terms of intraoperative blood loss (161.0 vs 548.7 mL, P< 0.001) and mean hospital days (12.7 vs 15.4, P=0.016). Total operative time was similar between groups (220.7 vs 205.2 min, in robotic and abdominal, respectively, P=0.263) and the mean docking and console time for RRH was 4.6 and 157.9 minutes. The number of retrieved lymph nodes and incidence of early/late postoperative complications were comparable, although there was higher incidence of wound related problems in the ARH group. The median follow-up was 33.5 months (range 1-69 months). Kaplan-Meier survival analysis demonstrated 87.2% and 88.5% PFS at 59 months for RRH and ARH, respectively (P=0.69). The OS was 96.2% at 66 months.

Conclusions: Robotic radical hysterectomy using 3 robotic arms can be considered a safe and effective therapeutic procedure for the treatment of early cervical cancer with improved operative outcomes. Survival outcomes are not compromised by robotic approach. Further studies are needed for long term oncological outcomes.
Poster Session II

HPV INFECTION IN EARLY PUERPERIUM

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Introduction: Participation of the HPV infection comes to be known to the onset of the cervical cancer deeply, and HPV sustained infection in the young group and pregnant women becomes the problem.

Objective: Evaluation of HPV infection in early puerperium.

Patients and methods: We carried out cervical smear in early pregnancy, cervical smear and HPV typing in early puerperium to 180 pregnant women got its consent and examined the change of cytodiagnosis views during pregnancy, the infection situation of the HPV virus in the puerpera.

Results: The cervical smear in early pregnancy was 171 NILM examples, 5 ASC-US examples (one HPV high risk in this), 4 LSIL examples. By the cervical smear carried out in puerperium, it was NILM 177 examples, ASC-US 9 examples (three HPV high risks in this), a AGC-NOS example, 3 inappropriate examples. By the cervical smear of the puerperium, we recognized the HPV infection of the high-risk type in 26 of 177 cases that were NILM. Of these, it was mixed infection of high risk and low risk HPV in three cases. With the HPV type, there were the most 52 types, and 11 cases, 58 type is eight cases, 39 type is 4 cases.

Conclusion: It was suggested that a lot of HPV infection of the high risk type existed even if judged to be NILM.
Poster Session II

PELVIC INSUFFICIENCY FRACTURE AFTER RADIOTHERAPY FOR CERVICAL CANCER

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Objective: Pelvic insufficient fracture (PIF) after radiotherapy for cervical cancer causes severe pain and spoils the quality of life of patients. This study was to investigate the clinical characteristics of PIF after radiotherapy for cervical cancer.

Methods: Among the patients who were diagnosed as uterine cervical cancer and treated with radiotherapy between 2002 and 2009 at Nara Medical University, 130 patients medical records were reviewed and assessed retrospectively.

Results: Fifteen patients (11.5%) were diagnosed as having PIF after pelvic radiotherapy. The median time from completion of radiotherapy to the detection of imaging studies was 16 months, with 6 patients (40%) diagnosed within 1 year and 10 patients (66.7%) within 2 years. Fourteen (93.3%) of PIF patients were postmenopausal, that was significantly fewer than non-PIF patients (64.3%). The portion of body weight < 50kg was lower in patients with fracture than in non-PIF patients (66.7% vs. 39.1% p=0.049). Among the PIF patients, pelvic pain developed in 11 patients, and 3 patients needed admission because of severe pain. Among these 11 symptomatic patients, 7 patients (63.6%) improved conservatively, but 4 patients (36.4%) had not adequate relief of symptom and their activity of daily life developed extremely worsen.

Conclusions: PIF was detected in a substantial proportion of the patients after radiotherapy for cervical cancer. Menopause and low body weight seemed to be the risk factor for PIF, and careful follow up should be needed in follow up for such patients.
Poster Session II

FAILURE OF TREATMENT IN PATIENTS WITH CERVICAL CANCER

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Background and aims: Cervical cancer is a preventable disease but still it has a mortality rate of 50% in our country. Primary treatment (surgery or radiotherapy) should be carefully planned to avoid morbidity and mortality. The aim of this study is to determine the failure of surgeon treatment that resulted to imposing combined method of surgery and radiotherapy.

Methods: Medical records all the referral patients with cervical cancer who had undergone radiotherapy after hysterectomy were reviewed retrospectively to determine the reasons for inappropriate hysterectomy. From 1988 to 2008, 93 files were submitted to postoperative radiotherapy at the our university tumor clinics of Ghaem and Omid hospitals that were eligible in terms of the patient's status at first reference and then follow-up after radiotherapy, surgeon errors, rate of recurrence or death and to evaluate factors related to survival were recorded. The cumulative 3- and 5-year disease-free survival (DFS) rate and overall survival rate (OS) were analyzed by Kaplan-Meyer test.

Results: Totally, surgeon errors were determined in 64 patients. The most error related to surgeon was inoperative surgery due to unawareness about cervical cancer. 3- and 5- year disease-free survival in the group without errors and in the group with errors were 86% and 64% in the group without failure vs. 53% and 47% in the group with failure was (P=0.05).

Conclusions: Determine and precise management with proper pretreatment evaluation is necessary to avoid inappropriate surgery.
Poster Session II

THE EFFECTIVENESS AND SAFETY OF ADJUVANT CHEMOTHERAPY IN PATIENTS WITH INTERMEDIATE-RISK EARLY STAGE CERVICAL CANCER AFTER RADICAL HISTERECTOMY

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Objective: To evaluate the effectiveness and safety of adjuvant chemotherapy in patients with intermediate-risk early stage cervical cancer after radical hysterectomy.

Methods: A total of 63 patients with intermediate-risk stage IB1-IIB cervical cancer treated in our institute were enrolled for retrospective analysis. These patients were treated with radical hysterectomy and pelvic lymphadenectomy followed by adjuvant chemotherapy. The indications for postoperative chemotherapy were based on pathological findings which were considered to be intermediate-risk factors for recurrence including deep stromal invasion(1/2), lymph vascular space involvement and large tumor size(>4cm). 21 patients with poorly-differentiated tumor were also treated with adjuvant chemotherapy. A variety of chemotherapeutic regimens were used and half of the patients received 5-FU and cisplatin.

Results: With an median follow-up period of 32.2 months (range 2.5-86.5 months) for survivors, the 2- and 3-year progression-free survival rates were 95.5% and 82.3%, respectively. Recurrence was observed in 4 patients. Three of them had pelvic recurrence and one had liver and lung metastases. Patients with stromal invasion less than 1/2 had significantly better progression-free survival than those with deep stromal invasion by Log-rank test ($P<0.05$). Toxicities were generally mild with Grade 3 neutropenia only in 2 (3.2%) patients.

Conclusion: Adjuvant chemotherapy for patients with intermediate-risk early stage cervical cancer seems to have equivalent effect on progression-free survival compared with adjuvant radiotherapy and could be a viable option. More aggressive treatment should be considered in patient with deep stromal invasion. A prospective randomized trial is needed to compare the effectiveness between adjuvant chemotherapy and radiotherapy.
Primary cancer of the vulva is rare accounting for less than 5% of all lower female genital tract cancers. Primary cloacogenic carcinoma of the vulva is extremely rare with less than 20 cases reported in English literature. These tumors are thought to arise from embryonic or ectopic rests of cloacogenic tissue. Here we present a case of metastatic cloacogenic carcinoma of the vulva.

Case: A 49 year old nulligravida woman presented with multiple small vulvar lesions. Metastatic workup showed spread to the lung and bilateral bulky inguinal and pelvic lymph nodes. Based on histology and immunoprofile of vulvar biopsy a metastatic adenocarcinoma from the gastrointestinal tract was suggested. After workup for gastrointestinal pathology was negative, she was treated with concurrent chemo-radiation to the vulva.

She received second line chemotherapy and laparoscopic bilateral pelvic lymph node debulking for persistent disease.

Discussion: Only a few cases have reported adenocarcinoma arising from cloacal remnants and majority of these were described small solitary non-metastatic tumors. Majority were treated with radical vulvectomy and bilateral inguinal lymph node excision. In our case radical vulvectomy was not possible due to entire vulva, lower vagina involvement.

Conclusion: Primary cloacogenic carcinoma of the vulva is very rare, based on literature, it is considered to be of indolent nature but in our case, the tumor was aggressive with metastatic spread. It provides evidence that although it is very rare it can be aggressive. It is important for pathologist and clinicians to be aware of this entity.
A CASE OF INVASIVE VULVAL EXTRAMAMMARY PAGET DISEASE WITH A MUCINOUS CARCINOMA COMPONENT

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Background: Extramammary Paget disease (EMPD) is a rare skin neoplasm that is characterized by intraepidermal proliferation of Paget cells. In advanced stage, it can invade the dermis typically with nodular, micronodular, or glandular pattern. We report an extremely rare case of EMPD that invades the dermis with a mucinous carcinoma component.

Case: An 80-year-old woman presented to our hospital with vulvar itching and pain that had developed over the past 7 years. Physical examination showed a vulvar and perianal erythematous plaque with pigmentation and a subcutaneous nodule in the left labia majora. Preoperative skin biopsy of the lesion revealed intraepidermal proliferation of Paget cells. Surgical excision of the affected area followed by skin reconstruction was performed. Histological examination of the resected skin revealed an infiltration of Paget cells forming solid nest with mucinous stroma in the labial dermis. Immunohistochemically, tumor cells were positive for CK7, CEA, MUC2 and MUC5AC, but negative for CK20, GCDFP-15, MUC6 and CDX2. No underlying associated internal and urogenital malignancy was identified. The diagnosis of invasive EMPD with a mucinous carcinoma component was made.

Conclusion: Vulvar and perianal EMPD and mucinous carcinoma are frequently associated with underlying genitourinary and colorectal carcinoma. For its precise diagnosis, close clinicopathological correlation, systemic work-up and immunohistochemical evaluation should be performed. Primary cutaneous mucinous carcinoma arising on the background of EMPD of the vulva and perineum is extremely rare and only 2 such cases were reported. Present case may represent an early stage of mucinous carcinoma development from EMPD.
Poster Session II

COMPLETENESS OF PATHOLOGY REPORTING AND IMPACT OF PATHOLOGY REVIEW IN POPULATION-BASED COHORT OF VULVAR CANCER PATIENTS

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Objectives: To describe the completeness of pathology reporting by specialist or general pathologists and the impact of a pathology review in a population-based cohort of vulvar cancer patients.

Methods: All cases of vulvar carcinoma diagnosed between 1998 and 2007 were identified using the provincial cancer registry. All pathology reports available from the registry for this cohort were abstracted for tumor details and prognostic factors. This analysis excludes groin specimens. Vulva specimens greater than 1.5cm were labeled “resections,” those smaller were labeled biopsies. Factors assessed for completeness of reporting were grade, size, depth, thickness, lympho-vascular space invasion (LVI), peripheral margin and deep margin.

Results: We identified 1,254 patients using electronic registry records. Preliminary analysis indicates 840 reports that fell into our definition of vulva resections: 534 from gynecopathologists, 306 from general pathologists. The percentage of reports with at least one variable missing was 16% for gynecopathologists and 45% for general pathologists. Depth of invasion was missing in 30% and 57% of reports for gynec and general pathologists respectively. 155 reports of a biopsy or resection reported by a general pathologist had a review of the same specimen by a gynecopathologist. 133 (86%) reports had a discrepancy on at least one factor. 50 (32%) reports changed from depth missing or < 1mm to being documented or increased depth of invasion.

Conclusions: Missing data was commonly found in reports from general and gynecopathologists. Pathology reviews changed important results in 86% of cases. This has important implications for treatment decision-making.
Poster Session II

PREVALENCE OF LYMPH NODES METASTASES IN CLINICALLY STAGES IB AND II VULVAR CANCER

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Objective: We analyzed the prevalence of inguino-femoral lymph nodes metastases in clinically early stages of vulvar cancer.

Material and method: Ten patients with IB-II FIGO stages vulvar cancer with no clinically and imagistic evidence of nodes metatases were treated in our clinic during a 15 months period (January 2011-April 2012). The surgical procedures consisted in radical vulvectomy plus uni- (2 patients) or bilateral (8 patients) inguino-femoral lymphadenectomy (depending on the primary lesion localization). In 2 patients we performed also a distal urethral resection (10-15 mm), in 3 a partial colpectomy and in one an unilateral extraperitoneal pelvic lymphadenectomy.

Results: The final pathological result was squamous carcinoma in 9 patients and carcinosarcoma in one. The prevalence of positive lymph nodes was 50% (5 out of 10 patients, between 1 and 5 positive nodes per groin, one bilateral and 4 unilateral). The median number of harvested lymph nodes was 13.0 per groin (between 7 and 27). Six patients developed some wound complications (infections, dehiscence, lymphocele etc.), but all were solved. Till now, all patients are alive and with no evidence of disease, but the follow-up period is short.

Conclusion: The prevalence of groin metastases in stages IB-II vulvar cancer is high. A thorough inguino-femural dissection seems necessary, despite the high incidence of wound complications.
Poster Session II

MARGIN STATUS AS PREDICTOR OF RECURRENCE IN SQUAMOUS CELL CARCINOMA OF THE VULVA: CHALLENGING THE 8 MILLIMETER RULE

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Objective: We aimed to investigate the relationship between tumor-free margin distance at the time of wide radical excision and recurrence in squamous cell carcinoma of the vulva.

Study design: We conducted a retrospective review of patients treated surgically for squamous cell carcinoma of the vulva between 1992 and 2009 at a single academic institution. Demographic, histopathologic, and follow-up records were collected. Patients were grouped by margin status at surgery. Patients with negative margins were subcategorized into those with closest margin < 5 mm, 5-8 mm, and > 8 mm. Patients whose pathology reports noted negative margins without quantification were placed in the < 5 mm group.

Results: Of the 86 patients identified, 76 had negative margins. Demographic data, including age, race, menopausal status, hormone replacement, and smoking status, were comparable between patients who recurred and those who did not. Recurrences were noted in 25% (10/40) of patients with < 5 mm negative margins, 38.5% (5/13) with 5-8 mm negative margins, and 17% (4/23) with > 8 mm negative margins (p=0.34). All disease recurrences were local. Patients with positive lymph nodes at surgery (16%) were distributed evenly among subgroups. There was no statistically significant difference in mean progression-free survival times or overall survival times among the subgroups.

Conclusion: In our population of patients with vulvar carcinoma, there was no statistically significant difference in recurrence rate, disease-free survival, or overall survival based on tumor-free margin distance, challenging the clinical benefit of 8 millimeter resection margins for vulvar carcinoma.
Poster Session II

LATE GI AND BLADDER TOXICITIES ASSOCIATED WITH TREATMENT FOR VULVAR CANCER

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Introduction: Limited literature exists to guide practitioners on counseling women about late toxicities associated with definitive therapies for vulva cancer (VC). We looked at the impact of treatment modalities (Surgery (Sx), radiation therapy (RT), chemotherapy (CTX) or combined therapies) on the development of late GI and bladder (BL) toxicities.

Methods: We estimated late toxicity rates in women diagnosed with VC using SEER-Medicare data between 1992-2005 (n=3,774). Late GI and BL diagnoses were identified if occurring 6-60 months after cancer diagnosis. Cox-proportional hazard models were used to estimate risk of late GI or BL toxicity stratified by treatment modality and cancer stage.

Results: Percentage of late GI toxicities was lowest among patients receiving RT alone (20.5%). In contrast, Sx alone, RT alone and combined RT/CTX have the lowest BL toxicity (~30%). The highest percentage of GI and BL toxicities occur in tri-modality therapy (54.3% GI and 34.3% BL). Toxicities by cancer stage were not significantly different.

Unadjusted hazard ratios, compared to Sx alone, show risk of developing late GI toxicity is higher for combination therapy (Sx/RT: HR 1.55, 95% CI(1.29-1.86); RT/CTX: HR 1.65,(1.19-2.29); Sx/RT/CTX: HR 2.21, (1.65-2.95)). The risk for late BL toxicities was highest for RT alone (HR 1.92,(1.25-2.93)), followed by tri-modality (HR 1.69, (1.17-2.42)) and Sx/RT (HR 1.57,(1.26-1.96)).

Conclusions: Tri-modality treatment for VC is associated with higher likelihood of late GI and BL toxicities. However, RT alone resulted in the highest likelihood of late BL toxicities. Patient counseling should include discussion of late toxicities related to VC therapies.
Poster Session II

A MULTIDISCIPLINARY APPROACH TO SURGICAL MANAGEMENT OF VULVAL DESMOID TUMOUR TO MAINTAIN THE COSMETIC APPEARANCE

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Background: Desmoid tumours are rare benign neoplasms originating from musculo-aponeurotic structures throughout the body. There are a number of reported cases of vulval desmoid tumours. Although benign in characteristic they can cause local infiltration resulting in significant deformity, morbidity or even mortality from pressure effects of the tumour. Surgical resection is challenging and management frequently involves a multidisciplinary approach combining the expertise of several surgical specialists. Radiation therapy has been used as a primary therapeutic option since desmoids are radio-sensitive. It is particularly useful in those patients who have underlying morbidities and are not suitable for surgery.

Case report: We report a vulval desmoid tumour presenting as a painful vulval mass. After histological diagnosis the tumour was resected via a lateral vaginal wall approach with multi surgical specialty input to obtain resection with adequate margins and good cosmetic appearance.

Conclusion: A number of surgical approaches have been described in literature for the resection of vulval desmoid tumour. We believe that the surgical approach adopted in this case allows for better cosmetic appearance and reduced postoperative recovery time. We identified intra-operative haemorrhage as a significant risk of surgical resection as previously highlighted in literature.
DETECTION OF MICROPARTICLES ISOLATED IN LYMPHATIC FLUID FROM PATIENTS WITH VULVAR CANCER

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Problem definition: Microvesicles such as microparticles (MP) and exosomes released from cancer cells are suggested to contribute to tumor progression and development of metastases via various mechanisms (figure 1). MP are present in urine, plasma and ascites, but have never been isolated from lymphatic fluid. If MP are present in lymph fluid, they may be involved in the development of lymph node metastases in vulvar cancer.

Objectives: To investigate whether MP are present in lymphatic fluid obtained from patients treated for vulvar cancer and to assess if their presence and characteristics are related to disease stage and treatment outcome.

Methods: Nine samples of lymphatic fluid from seven patients with vulvar cancer treated with complete lymph node dissection were included. MP were isolated by centrifugation, analysed with flow cytometry and identified based on their size, density and exposure of cell-specific monoclonal antibodies.

Results: Lymphatic fluid contained MP from different cell types (table 1). The majority of MP were derived from granulocytes (figure 2). Surprisingly, B and T cell-derived MP were hardly detectable. No significant differences were found between the number of MP and disease stage and treatment outcome.

Conclusion: MP are present in human lymphatic fluid. Further studies are needed to evaluate their function and possible contribution to the development of lymph node metastases in vulvar cancer.
Figure 1: Functions of microparticles and exosomes in gynaecological malignancies
Abbreviations: MV = microvesicles, L1CAM = L1 cell adhesion molecule, MMP = matrix metalloprotease, PS = phosphatidylserine, TF = tissue factor, TGF-β = Transforming growth factor beta

[Figure 1: Functions of microparticles and exosomes]
<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Antibody</th>
<th>Number of MP</th>
<th>Number of MP</th>
</tr>
</thead>
<tbody>
<tr>
<td>T helper cells</td>
<td>Anti-CD4-FITC</td>
<td>ND</td>
<td>0-38 x 10^3</td>
</tr>
<tr>
<td>B-cells</td>
<td>Anti-CD20-PE</td>
<td>4 x 10^3</td>
<td>0-71 x 10^3</td>
</tr>
<tr>
<td>Monocytes</td>
<td>Anti-CD14-FITC</td>
<td>15 x 10^3</td>
<td>0-282 x 10^3</td>
</tr>
<tr>
<td>Endothelial cells</td>
<td>Anti-CD62e-PE</td>
<td>6 x 10^3</td>
<td>0-148 x 10^3</td>
</tr>
<tr>
<td>Squamous cells</td>
<td>Anti-CD227-FITC</td>
<td>1 x 10^3</td>
<td>0-45 x 10^3</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>Anti-CD235a-FITC</td>
<td>28 x 10^3</td>
<td>0-4129 x 10^4</td>
</tr>
<tr>
<td>Granulocytes</td>
<td>Anti-CD66b-FITC</td>
<td>337 x 10^3</td>
<td>36-2666 x 10^3</td>
</tr>
</tbody>
</table>

[Number of MP in lymphatic fluid]

**Figure 2: MP derived from granulocytes Anti-CD-66b-PE**

[Figure 2: MP derived from granulocytes]
Poster Session II

NODAL STATUS IN RELATION TO SIZE & GRADE OF THE TUMOUR IN PATIENTS SURGICALLY TREATED FOR VULVAL CANCER

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Vulval Cancer is a rare Gynaecological Cancer. Surgical Treatment is still the standard therapy for those operable / resectable patients.

Objective of the study: To determine the Lymph node status in relation to size & grade of the tumour, to define prognostication & treatment outcome.

Material and methods: Between January 2005 & April 2012, the case records revealed 78 patients with Carcinoma Vulva. Of these 78 patients, 55 patients underwent Radical Vulvectomy with Inguinofemoral block dissection. Surgico-pathological staging was determined & nodal status was studied in relation to size, & grade of the tumour. The data was analysed by SPSS chisquare data base.

Results: The mean age was 57.54 years (ranged between 30-85 years). The size ranged between 1.5 cm - 15cms, the size of the tumour perse is not significant (p=0.72), however the high grade (3) & tumour size of more than 4cms increases the chances of nodal involvement with or without Perinodal spread (p=0.03)Majority of the patient had wound dehiscence & groin wound gapping, thus delaying for postoperative adjuvant therapy.

Conclusion: The present study indicates that the patients with carcinoma vulva can be treated with Radical wide excision / Radical Vulvectomy for the loco regional control followed by concurrent Radiotherapy / Chemoradiation in all the high risk patients with vulvar cancer, thus the complaints & improvement in survival without much morbidity can be considered with more multicentric study.
P
er Session II

LARGE B CELL LYMPHOMA OF THE VAGINA WITH SPINDLE-CELL MORPHOLOGY

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Introduction: Non-Hodgkin’s lymphomas (NHL) involve the female genital tract, however rarely is it the primary site of malignancy. We present a case of a 38 year old woman who developed a primary vaginal NHL. This case highlights the need to consider NHL in the differential diagnosis of vaginal masses.

Case summary: A 38 yr old woman was referred after finding a raised area on her vagina. Two small punch biopsies showed changes compatible with HPV. 3 months later at review, the lesion had grown to form a definite palpable lump. A wedge biopsy, EUA with sigmoidoscopy was performed which was normal. Histology revealed a large B cell lymphoma with a rare spindle cell pattern. Pelvic MRI showed a poorly defined mass (7cm x 8.5cm x 7.8cm) along the left vaginal wall extending into the left hemipelvis and suspicious of uterine involvement. There was no pelvic lymphadenopathy or metastatic disease. The final diagnosis was a bulky stage 1c high grade vaginal NHL and treatment was commenced with 6 cycles of CHOP chemotherapy and radical radiotherapy and she remains well to date.

Discussion: Lymphomas of the genital tract are rare but should be considered in women of all ages presenting with an atypical mass. Pelvic MRI imaging and biopsy at an early stage will prevent delayed diagnosis. Spindle cells are formed during abnormal mitosis, leading to a malignant change. An awareness of vaginal NHL is necessary in order to prevent potential delay or misdiagnosis which leading to inappropriate treatment.
Poster Session II

INTRAOPERATIVE CARDIAC ARREST DURING RADICAL VULVECTOMY UNDER COMBINED SPINAL-EPIDURAL ANESTHESIA: A CASE REPORT

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Introduction: Vulvar carcinoma is a rare disease, comprising only 3-5% of all gynecologic malignancies. Surgical treatment may be associated with perioperative complications arising from the procedure itself or administration of anesthesia. Herein, we report a case of an intraoperative cardiac arrest, which occurred during radical vulvectomy (RV) performed under combined spinal-epidural anesthesia. To the best of our knowledge, it is the first report of cardiac arrest that occurred during RV operation.

Case: A 78-year-old woman referred to our institution with vulvar itching. Vulvar biopsy revealed squamous cell carcinoma. Radical vulvectomy was planned. She had a coronary angiography 3 years ago, which was reported as normal. She also had diabetes mellitus and hypertension. Anesthesiologists classified her preoperative risk as ASA-III. Intraoperatively, combined spinal-epidural anesthesia was induced, using 10 mg intrathecal bupivacaine from L3-4 level. At the 60th minute of the operation, severe bradycardia developed and rapidly progressed to cardiac asystole. Precordial thump was followed by external chest compressions, and tracheal intubation. Adrenaline and atropine was administered. Sinus rhythm was restored after 2 minutes of resuscitation. Within 10 minutes, ventricular fibrillation developed, which responded to defibrillation. The operation was rapidly commenced. Postoperative follow-up was uneventful, and the patient fully recovered.

Conclusion: Intraoperative cardiac arrest is an extremely rare and unexpected complication, occurring in <0.03% of non-cardiac surgeries. Although vulvar surgery is generally considered safe, life threatening conditions may occur during surgical treatment.
Poster Session II

VULVAR CARCINOMA IN PUERPERIUM: CASE REPORT

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Background: Invasive squamous cell carcinoma of the vulva is primarily a disease of postmenopausal women and thus is rarely associated with pregnancy.

Case: A 37-year-old woman presented with 3x 3 cm vulvar lesion 2 weeks after cesarean, subsequent biopsy revealed squamous cell carcinoma. She had a history an ulcer on her left labia minor at the third month of pregnancy. She was treated by a modified radical vulvectomy and bilateral groin lymphadenectomy.

She received no additional therapy. Two year later, she had no recurrence of the disease.

Conclusion: This case emphasizes the need to consider malignancy as a differential diagnosis in vulvar lesions of pregnant young women.
Poster Session II

AN ANALYSIS OF THIRTY-ONE CASES WITH PRIMARY VAGINAL MALIGNANT MELANOMA

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Objective: To investigate the diagnosis, treatment and prognostic factors of primary vaginal malignant melanoma.

Methods: Clinical data of 31 patients with primary vaginal malignant melanoma treated in Sun Yat-sen University Cancer from March 1970 to June 2005 were retrospectively analyzed.

Results: The average age was 53 years. The main symptoms were vaginal discharge and bleeding tumor. Tumors were mostly cauliflower like. The interval from onset of symptoms to treatment averaged 18.6 months. The 5-year overall survival rate was 32.3% and the median survival time was 20.2 months. Twenty-three patients applied with surgical-based treatment while 8 patients underwent non-surgical treatment. The average overall survival (OS) was 44.0 months in the surgical group versus 18.2 months in the non-surgical group. In the surgical group, there were 12 patients received more aggressive surgeries with hysterectomy and 11 patients underwent less aggressive surgeries. However patients had more aggressive surgeries had poorer prognosis. Eighteen patients were treated followed by immunotherapy while the other 13 did not. The average overall survival (OS) was 47.2 months in immunotherapy group and 19.7 months in non-immunotherapy group. Multivariate analysis showed that surgical approaches and tumor types (P < 0.05) affected overall survival time of patients.

Conclusion: For patients with vaginal melanoma in early stage, local extensive excision followed by immunotherapy may achieve good prognosis.
Poster Session II

TREATMENT OPTIONS OF VULVA CANCER


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Objectives: Vulva cancer is rare and accounts for 3-4% of gynecological malignant tumors. A radical vulvectomy was previously believed to be the only effective treatment but has recently been replaced by more individualized treatments from the standpoint of QOL. In the present study we examined outcome of individualized minimal invasive surgery, such as simple vulvectomy including unilateral or bilateral inguinal lymph node biopsy.

Methods: Medical records of patients with Stage I to IV vulvar cancer from 2005 to 2011 were retrospectively examined. Survival rate was analyzed using the Kaplan-Meier method.

Results: The 5 year survival rates were 100%, 26.8%, and 59.7% for 4 cases with Stage I/II, 7 cases with Stage III/IV, and total of 11 cases, respectively. Surgery combined with chemotherapy and/or radiotherapy was successful for some of the stage III/IV patients.

Conclusions: Minimal invasive surgery may be a standard therapy for early-stage vulvar cancer.
Poster Session II

SENTINEL NODE (SN) BIOPSY IN EARLY STAGE SQUAMOUS CELL CANCER (SCC) OF THE VULVA

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Background: To assess the safety and feasibility of using SN biopsy in the management of patients with early stage (1B) SCC of vulva.

Methods: Retrospective review of clinical records of all patients with SCC of the vulva treated from 2005 to 2010 with SN biopsy only, using the standard technique of pre operative lymphoscintigraphy and intraoperative blue dye injection with ultrastaging done by pathologist to exclude micro metastasis.

Results: 25 patients were included with a mean (SD) age of 64 (17.1) years. Median tumour size was 1.6 cm (range: 0.5-6cm). Sixteen (64%) and 9 (36%) patients had lateral and midline lesions. Overall, 49 groins were dissected and SN were identified in all. Seven patients had positive SN and 18 patients had negative SNs identified. All 7 patients with positive SNs received adjuvant radiotherapy. Median follow-up was 25.7 months. One patient with negative SN was lost to follow up while 2 patients with positive SN died of intercurrent illness. Three of the 7 patients with positive SN had recurrences in the vulva (12.5%). One of the 18 patients with negative SN had a recurrence in the contra lateral groin (5.8%) 17 months later. However this patient had a 3.8 cm left lateral lesion (2 cm away from midline) with a negative SN identified on the ipsilateral side.

Conclusion: In our experience SN detection in the management of patients with early stage SCC of vulva seems safe and feasible.
Poster Session II

PRIMARY MALIGNANT MELANOMA OF THE VAGINA

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The incidence of malignant melanoma (MM) of the vagina is 0.46 per million women. The patients are often at age 60-70 years and the most common primary symptom is vaginal bleeding.

This previously healthy 77-year old woman presented with vaginal bleeding. Examination revealed a 2 centimetre tumorous lesion just inside the vagina in near relation to urethra (picture 1). FDG PET CT showed high activity in the lower vagina only (picture 2). Biopsy showed MM of nodular type.

The patient went through pelvic exenteration. The histopathological report confirmed MM of nodular type with an ulcerated surface (picture 3). The diameter was 25 mm and the depth of invasion 18 mm, immunoreactive for S-100, melan-A, MSA and MITF. Mitotic index was 10 mitosis/10 HPF.

The patient received no kind of adjuvant therapy. Seven months later she unfortunately had local recurrence.

Vagina is a rare location of primary MM and the literature is mostly based on case reports, some suggest the use of prognostic factors as mitotic index < 6 mitosis/10 HPF, tumour type and size.

The prognosis is poor with 5-year survival rates between 5-25%. Complete resection is important, but exenterative surgery has not shown a better overall survival (OS) compared to more conservative radical excision. Postoperative radiotherapy may reduce the risk of local recurrences, but does not increase OS. Adjuvant chemotherapy has not shown any significant effect on OS.

There is a need for larger cohorts of patients to identify prognostic factors and create useful guidelines on treatment recommendations.
Poster Session II

EFFICACY OF FOCUSED ULTRASOUND IN THE TREATMENT OF VULVAR INTRAEPITHELIAL NEOPLASIA

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Objective: To investigate the clinical effectiveness, safety, and feasibility of focused ultrasound in the treatment of vulvar intraepithelial neoplasia (VIN).

Methods: A total of 8 patients with clinically diagnosed VIN ranging in age from 31 to 71 years voluntarily underwent focused ultrasound treatment. Among them, 6 cases were in stage I and 2 cases were in stage II. CZF model ultrasound manufactured by Chongqing Haifu (HIFU) Technology Co., Ltd was used. Patients were anesthetized locally with lidocaine. Continuous linear scanning was then applied for 15 to 30 min. All patients tolerated the procedure well. Changes of clinical features and histology of the lesions were assessed during regular follow-up visits.

Results: At six-month follow-up, vulva lesions in 6 patients returned to normal skin histology on biopsy. One patient showed vulva chronic inflammation, and the other had vulva squamous hyperplasia. None of the patients developed invasive carcinoma of the vulva during the 18 to 48 months of follow-up period. Two patients complained local pruritus one week after treatment, which were alleviated with anti-inflammation medication and local care. Three patients presented with superficial second-degree burn which healed spontaneously with local wound care.

Conclusion: This small series suggest that focused ultrasound is effective in the treatment of early stages of VIN with excellent preservation of form and function and minimal morbidity. It can be performed repeatedly and is particularly useful for treating multifocal lesions such as VIN.
**Poster Session II**

**DESCRIPTION OF PATIENTS WITH VULVAR CANCER FROM 2001-2005**

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**Background and aims:** Analyzing the characteristics, treatment and management of patients with vulvar cancer.

Vulvar cancer is a rare tumor type. This study analyzes our experience in treatment and follow up with these patients.

**Material and methods:** We identified all patients with vulvar cancer treated at the HMI of Granada between 2001 and 2005, with a total of 16 patients.

**Results:** We identified 16 patients with a mean age of 75.5 (69-82).

Half of the patients had previous premalignant vulvar lesions at diagnosis.

25% of patients had affected the midline.

All patients had pathology of squamous cell carcinoma, except 2 patients (paget).

Clinical stages were: I (A or B) = 87.5%; III=12.5%.

In relation to treatment: The surgery of choice was vulvectomy with lymphadenectomy with separated incisions (62.5%). The remaining patients underwent vulvectomy only.

Radiation therapy (external type) was performed for 4 patients (25%).

At follow-up after 5 years, 62.5% were alive without disease, 25% had died of cancer and 12.5% had died of intercurrent diseases.

Disease-free survival was 11 months, overall survival was 35.5 months.

**Conclusion:** Patients with this type of cancer used to be of very old-age at diagnosis.

Most of the tumors were diagnosed at an early stage.

Monitoring shows a good performance in most cases.
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Poster Session II

THREE CASES OF PRIMARY VAGINAL CARCINOMA

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Introduction: Primary vaginal carcinoma is rare, constituting about 3% of gynecological cancers. Due to rarity of disease standardized treatment protocols are lacking. This leads to management difficulties in clinical practice.

Aims and objectives: In our Institute Dharamshila Cancer and Research Centre, Delhi; in last one year three patients presented with primary vaginal carcinoma. The clinical data and management results are presented to evaluate effectiveness of the protocols followed in these patients.

Results: Clinical and Treatment Details are given in Table No 1:

<table>
<thead>
<tr>
<th>S. no</th>
<th>Age of patient</th>
<th>Size and location of disease</th>
<th>Histo-pathological Type</th>
<th>Primary modality of treatment</th>
<th>Response to primary treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67 yrs</td>
<td>Size: 4-5 cms, anterior vagina with complete procidentia (malignant transformation of decubitus ulcer)</td>
<td>Poorly differentiated carcinoma</td>
<td>Radiotherapy (resistant), hence primary radical hysterectomy with upper 2/3rd vaginectomy was followed by palliative chemotherapy</td>
<td>Poor, patient progressed, DFS: Nil</td>
</tr>
<tr>
<td>2</td>
<td>61 yrs</td>
<td>Size: 4cms, On left vaginal wall, 2 cms below cervix</td>
<td>Small cell carcinoma of neuroendocrine variety</td>
<td>Primary chemotherapy followed by radiotherapy</td>
<td>Good</td>
</tr>
<tr>
<td>3</td>
<td>60 yrs</td>
<td>Size: 5-6cms involving upper 2/3rd of anterior vaginal wall</td>
<td>Moderately differentiated Squamous cell carcinoma</td>
<td>Concurrent Radiotherapy and chemotherapy followed by interstitial needle implants in anterior vagina</td>
<td>Good</td>
</tr>
</tbody>
</table>

Conclusion: Best individualised treatment as guided by scant literature in each histopathological variety of primary vaginal carcinoma is needed. Aggressive varieties like Poorly differentiated and
small cell varieties require primary systemic chemotherapy. Radiotherapy or surgery are to be timed as per need. In squamous cell variety interstitial needle implants is excellent modality to give radiation boost dose to vagina.
Poster Session II

INTRA-ARTERIAL CHEMOTHERAPY COULD OBTAIN SUFFICIENT LOCAL CONTROL FOR ADVANCED VAGINAL CANCER

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Introduction: Radiotherapy or concurrent chemoradiotherapy (CCRT) is usually recommended for advanced vaginal cancer. However, there is a lack of evidence supporting specific administration methods for advanced vaginal cancer. We are reporting our experiences of three cases in which we were able to obtain sufficient local control through the administration of intra-arterial chemotherapy (IA) prior to the administration of CCRT for advanced vaginal cancer.

Method: IA(CDDP100mg/body+5-FC1000mg/body) was administered on three patients with stage IVb of vaginal cancer followed by CCRT. The therapeutic value of our method of treatments was evaluated using RECIST.

Results: The therapeutic value of treatments for three patients was as follows; one CR case, one PR case and one PD case. In the CR case, no recurrence was observed in the 4 months. Moreover, the PFS of the PR case has reached 19 months. On the other hand, there was recurrence in the inguinal lymph node in one of the patients who led to their case being evaluated as PD, but the patient is currently in no evidence of diseased due to additional chemotherapy at a later stage. In addition, in all three patients, the local area was determined to be CR after the administration of IA and no local reoccurrence has been currently observed in any of the three patients including PD case.

Conclusion: In this patient group, outcomes were better using IA treatment in terms of local control. Accordingly, IA might be one of the other optional treatments for advanced vaginal cancer.
Poster Session II

FLUORESCENT DIAGNOSIS OF A PREMALIGNANT LESIONS AND CANCER OF VULVA

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Background: Fluorescent diagnosis (FD) is a modern diagnostic option based on the detection of distinctive fluorescence of normal and pathological tissue. The aminolevulinic acid (5-ALA) - based fluorescence diagnosis has been found to be promising for an early detection and demarcation of the vulvar diseases.

Aim: In this study we have analysed sensitivity of the FD at 80 patients (age 25 - 60 years) with vulvar disorders, vulvar intraepithelial neoplasia (VIN) I - III, and vulvar carcinoma stage IA.

Methods: 5-ALA was topically applied to the vulva which is preferentially absorbed and induces protoporphyrin IX accumulation in neoplastic tissue. After 4 hours the vulva skin was illuminated from laser using certain wavelengths. Use of 5-ALA by us allowed to perform diagnostic research - fluorescent spectroscopy with additional visualization of pre-malignant lesions of the vulva. Procedure of registration of a fluorescent spectrum occupied some seconds. After the FD biopsies were taken. Macroscopic appearance, fluorescence pattern and histology of the lesions were compared.

Results: Histological assessment of the fluorescence-directed biopsies revealed: from 80 patients at 22 patient diagnosis from VIN III to vulva cancer I A stage that has made 27,5 % is established. At the others 58 patients are revealed lichen sclerosus and squamous cell hyperplasia.

Conclusion: The FD becomes a valuable, non-invasive diagnostic tool that lowers the amount of false negative diagnosis in cases of VIN and vulvar cancer.
Poster Session II

**P53 AND KI-67 EXPRESSION IN A PREMALIGNANT LESIONS AND CANCER OF VULVA**

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**Background:** P53 and Ki-67 expression is an important molecular mechanism in carcinogenesis, which has also been demonstrated for vulvar carcinoma.

**Aim:** To evaluate p53 and Ki-67 changes in vulvar carcinogenesis, we analyzed new tumour markers expression in vulvar carcinoma, vulvar intraepithelial neoplasia (VIN), lichen sclerosus (LS) and squamous cell hyperplasia (SH).

**Methods:** 10 women with vulvar cancer, 10 woman with VIN I-III and 10 woman with LS and SH have been enrolled to the study. Investigation included assessment of the proliferative activity of cancer cells and expression of the tumor suppressor protein in formalin-fixed paraffin-embedded tumors, using monoclonal antibodies to p53 and Ki-67.

**Results:** Vulvar epithelium of LS and SH showed low Ki-67 staining (1-25%). Its expression was essentially increased at VIN and was maximal in vulvar cancer - 85%. P53 increased stepwise from LS and SH to vulvar carcinoma. However we didn’t reveal accurate dependence between over expression p53 and Ki-67.

**Conclusion:** In vulvar cancer, the expression of Ki-67 provides significant information about prognosis. The routine evaluation of Ki-67 level could be a useful tool in identification of patient with more aggressive disease and contribute to a better therapeutic approach.
Poster Session II

PERSISTENT CARCINOMA IN SITU OF A COLONIC NEOVAGINA: A CASE REPORT

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Case report: A 42-year-old woman presented with persistent neovaginal bleeding. In early childhood a hysterectomy, bilateral salpingo-oopherectomy and total vaginectomy was performed for a uterine sarcoma botryiodes, and she subsequently underwent a vaginal reconstruction using the sigmoid colon in her late teens. Examination under anaesthesia revealed a suspicious looking mass of the posterior wall of the neovagina. A wide local excision was performed and histology was consistent with large intestinal mucosa showing high-grade dysplasia. Repeat biopsies following argon beam ablation at 6 monthly intervals have confirmed persistent high-grade dysplasia. The patient continues to be managed conservatively with annual follow up.
Discussion: Carcinoma in situ of the neovagina is rare and has the potential to progress into invasive disease. The underlying pathophysiology for this transformation is not well defined. The possible role of HPV infection in the aetiology of neovaginal dysplasia is discussed. We also consider whether conservative management could be an optimal treatment in women of reproductive years.

Conclusion: This case report reinforces that transplanted colon, still retains oncogenic potential and may in fact be at greater risk of development of carcinoma due to exogenous influences. For this reason, all patients who have undergone neovaginal construction should undergo annual follow-ups,
which should include a pelvic examination and smear analysis. In addition, HPV testing may also be of benefit given the potential association of neovaginal dysplasia with HPV infection.
Poster Session II

LATE ISOLATED VULVAR RECURRENCE OF SIGMOID COLON CANCER MIMICKING PRIMARY VULVAR CANCER: A CASE REPORT

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Metastases to the female genital tract from other cancers are rare and the most common extra-genital primary regions are to breast and gastrointestinal carcinomas. In such cases, ovaries are most often affected, while isolated vulvar metastasis is extremely uncommon and constitutes 5-8% of all vulvar tumours. Discrimination of the metastatic lesion from primary carcinoma is critical for both management and prognosis. Lymph node involvement and the stage of disease strongly correlated with outcomes of primary cancers whereas metastatic lesions tend to accompany widespread diseases and generally have poor prognosis. A 53-year-old postmenopausal multigravida woman was admitted to the gynecology department with the complaint of bloody vaginal discharge for 1 week and newly recognized irregular vulvar mass ongoing for 2 months. After investigations and biopsy, vulvar adenocarcinoma was reported as pathology report. Immunohistochemistry revealed vulvar metastasis of the colon adenocarcinoma. In summary, metastatic lesions of the vulva may accompany further malignancies as a result of widespread disease and generally associated with worse outcome. Patients especially with prior malignancy are under risk of late recurrences and should be carefully evaluated.
Poster Session II

SURVIVAL OF SURGICALLY TREATED PATIENTS DIAGNOSED WITH PRIMARY INVASIVE VULVAR CANCER IN A GREEK MAJOR CANCER HOSPITAL BETWEEN 2000-2005

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Background and aims: Vulvar cancer is a rare disease accounting approximately 4% of malignancies of the female genital tract. We investigated the overall survival of our surgically treated patients diagnosed with primary vulvar cancer.

Methods: The pathology database of our hospital was searched for patients diagnosed with primary vulvar cancer between 2000-2005. Patient’s notes and pathology reports were reviewed. Data for analysis included age, histological type, grade, stage, surgical margins and number of positive lymph nodes. Only patients who underwent surgery as primary treatment were included in the study.

Results: 26 patients were included in the study. Mean age of diagnosis was 72.4 years (38-90). Squamous cell carcinoma was found in 23 patients (84.6%), melanoma in 1, sarcoma in 1 and adenocarcinoma in 1 patients respectively. The median number of groin lymph nodes removed was 12. 5-year follow-up data were available for 21 patients. Stage I 5-year survival was 69.2%, stage II 50%, stage III 33.3%, stage IV 0% as estimated by the Kaplan-Meier test. The 5-year survival rate for those with positive groin nodes was 33.3%.

Conclusions: The number of positive groin nodes is the most important prognostic variable. The total number of our patients is relatively small in order to draw safe conclusions and this fact might explain the small deviations observed from published data. The rarity of the disease denotes the need for larger studies.
Poster Session II

A RARE CASE OF AGGRESSIVE ANGIOMYXOMA OF VULVA

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Introduction: Aggressive angiomyxoma is a rare, mesenchymal neoplasm, locally aggressive soft tissue tumor that has high propensity for local recurrence. It has estrogen and progesterone receptors explaining its propensity in females. It involves mainly the pelvis, vulva, perineum, vagina and urinary bladder in adult women in the reproductive age. Although this tumor has bland histological features, it has propensity for local recurrence (30-72%), sometimes even decades later. Considering its locally aggressive nature, appropriate management and long-term follow-up is necessary. It commonly presents as a painless, poorly circumscribed gelatinous vulvar mass and clinically simulates a Bartholin gland cyst or an inguinal hernia.

Case: We describe a case of 32 year-old patient who presented with slowly growing mass in the left labia majora. She had history of similar swelling in the past which was excised one year ago. The mass measured 15cm by 10cm arising from left labium major. It was a well defined mass with normal overlying skin. As the tumor was extending near rectum posteriorly and urethera anteriorly, radical excision was not possible. The cut surface was white, homogeneous and had a gelatinous appearance. The histopathology confirmed angiomyxoma. The patient is under follow-up. She will be evaluated for the unexcised tumor mass and will be considered for gonadotrophin agonist therapy.

Conclusion: Aggressive angiomyxoma merits wider recognition as a distinctive tumor type and a long-term follow-up is required.
Poster Session II

BRAIN AND LUNG METASTASIS AFTER PRIMARY TREATMENT OF BARTHOLIN'S GLAND ADENOID CYSTIC CARCINOMA: A CASE REPORT

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A 48-year-old premenopausal female patient was delivered adjuvant pelvic and inguinal radiotherapy after prior complete left Bartholin's gland tumor excision and inguinal lymph node dissection for adenoid cystic carcinoma of Bartholin's gland with one metastatic inguinal lymph node. Initial whole body Positron Emission Tomography scan did not detect any disease extension in the lung, liver, brain or bone. After cure, regular follow-up visits were organized with CT scans every 6 months.

Two years after primary treatment, she complained of acute headache, hypoacusia, decrease in visual acuity, and a decrease in right leg muscle strength. Cranial MR imaging demonstrated three cystic brain lesions with associated perifocal oedema. Chest and abdomen CT scans and MR of the pelvis did not find any metastatic or residual disease elsewhere. Physical examination found no local recurrence.

Stereotaxic brain biopsies with pathology examination revealed the presence of adenoid cystic carcinoma metastasis. The patient thus received 30 Gy of brain radiotherapy but three months later, the brain lesions did not decrease in size and left mid lobular lung lesions appeared on the chest CT scan. A mid left lobe lung excision was undertaken followed by chemotherapy consisting of cisplatin and adriamycin. The brain lesions are still progressing with increased oedema and the appearance of seizures.

There is no consensus on the optimal treatment of metastatic adenoid cystic carcinoma of Bartholin's gland. This case report shows that radiotherapy alone is not sufficient.
Poster Session II

HIGH GRADE VAGINAL INTRAEPITHELIAL NEOPLASIA (VAIN): WHAT DO YOU DO WHEN CYTOLOGY IS ABNORMAL BUT VAGINOSCOPY IS NORMAL?

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¹Northern Gynaecological Oncology Centre, ²Department of Pathology, Queen Elizabeth Hosiptal, Gateshead, UK

Background: VAIN is a rare premalignant condition for which primary surgical treatment is often performed in high grade (HG) cases. Evidence supporting the role of conservative management is lacking.

Objective: To determine the role of conservative management in HG VAIN.

Methods: Retrospective observational study of women with HG VAIN on biopsy referred to the Northern Gynaecological Oncology Centre, Gateshead from 1995 until 2011.

Outcome measures 1) Progression to cancer, 2) treatment remission, 3) recurrence, and 4) progression-free follow-up when cytology is abnormal but vaginoscopy is normal.

Results: Of 100 women referred, 69 underwent primary treatment. Twenty-two (32%) had treatment failure within 12 months and 7 recurrences (15%) occurred after 12 months.

The remaining 31 patients were managed conservatively. None progressed to cancer after a total follow-up period of 121 women years.

Overall rate of progression to cancer was 3%. All were detected amongst the primary treatment group at a median of 40 months (range 8-249 months).

There existed 43 episodes when normal vaginoscopy was accompanied by abnormal cytology post-treatment. Of 24 cases (56%) with low grade cytology no cancers developed and recurrence of HG VAIN occurred in 7 cases (29%) at median 17 months (range 2-110 months). Of 19 patients (44%) with HG cytology, 1 cancer developed at 133 months and 14 (74%) developed recurrence at median 17 months (range 2-21 months).

Conclusions: This, the only study of HG VAIN alone, demonstrates HG recurrence in 74% of cases post-treatment when normal vaginoscopy is accompanied by HG cytology. All recurrences occurred within 2 years.
Poster Session II

HIGHER NODAL COUNT AND LOWER COMPLICATION RATES WITH VERTICAL GROIN INCISION INGUINOFEMORAL LYMPHADENECTOMY (IFL) IN VULVAL CANCER (VSCC)
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Background and aims: In our institution both transverse and vertical approaches are performed for groin dissection in VSCC. We have reported previously that lymph node count can be used as a surrogate for the adequacy of IFL with an adequate count defined as eight or more nodes. This study examines: lymph node count, groin infection, lymphedema, lymphocyst, and DVT rates according to the type of groin incision.

Methods: All cases of VSCC where IFL was performed since 2009 were recorded. Nodal debulking cases were excluded. Rates of inadequate nodal count and complication type were analysed.

Results: Between 2009 and 2012 41 IFLs were performed in 24 patients. (See table).

<table>
<thead>
<tr>
<th></th>
<th>Vertical (VI)</th>
<th>Transverse (TI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>9</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Groins</td>
<td>16</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Median node count per groin</td>
<td>9</td>
<td>7</td>
<td>0.083</td>
</tr>
<tr>
<td>Inadequate IFL (&lt;8) per groin</td>
<td>2/16 (12.5%)</td>
<td>14/25 (56%)</td>
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</tr>
<tr>
<td>Groin infection (patients)</td>
<td>4/9 (44.4%)</td>
<td>9/15 (60%)</td>
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<tr>
<td>Lymphoedema (patients)</td>
<td>1/9 (11.1%)</td>
<td>7/15 (46.6%)</td>
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</tr>
<tr>
<td>Lymphocyst (patients)</td>
<td>2/9 (22.2%)</td>
<td>8/15 (53.3%)</td>
<td>0.209</td>
</tr>
<tr>
<td>DVT (patients)</td>
<td>0/9 (0%)</td>
<td>2/15 (13.3%)</td>
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</tr>
</tbody>
</table>

[Results]

Conclusion: Vertical compared to transverse groin incision was associated with higher node count and fewer complications. Importantly rates of inadequate lymphadenectomy were significantly lower in the VI group. Further studies are needed to validate these findings including multivariate analyses in a larger series and assess morbidity, recurrence and survival.
Poster Session II

CONSERVATIVE TREATMENT AND LONG-TERM FOLLOW UP OF ENDODERMAL SINUS TUMOR OF THE VAGINA

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Objective: Six cases of endodermal sinus tumors (EST) of the vagina were reported focusing on the results of conservative treatment and outcome of long-term follow up.

Methods: We reviewed a cohort of six cases with EST of the vagina diagnosed and treated in our hospital. CT scan, detection of serum AFP level, EUA and biopsy were performed before and after treatment to evaluate the tumor status. The diagnoses of EST of the vagina were confirmed by pathological and imaging findings. All patients were treated with bleomycin, etoposide and cisplatin (BEP) combination chemotherapy alone. Complete remission (CR) includes the normal level of serum AFP, no tumor detected by CT scan and the negative result of pathology. Long-term follow up were carried out according to our regulation.

Result: The mean onset age was 18.2 months. The average tumor size was 4.5cm. Serum AFP level was markedly elevated before treatment and decreased dramatically after chemotherapy and drop to the normal level after two to three courses of chemotherapy (average 2.5 courses). The patients received averagely six courses of BEP chemotherapy and all the six patients obtained CR. The mean follow-up time is 75.5 months and there was no evidence of recurrent disease.

Conclusion: The result of this conservative treatment for EST of the vagina is excellent. BEP chemotherapy without surgery should be considered as a good choice of treatment for patients with EST of the vagina. Closely follow up with serum AFP level, imaging tests and physical examination in the first two years are recommended.
Poster Session II

PREGNANCY AFTER FERTILITY-SPARING SURGERY FOR CLEAR CELL ADENOCARCINOMA OF THE VAGINA

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Akdeniz University, School of Medicine, Antalya, Turkey

Objective: Clear cell adenocarcinoma of the vagina is traditionally treated with radical surgery and/or radiation therapy. However, clear cell carcinoma of the vagina usually affects women in reproductive age and desiring fertility. Radical trachelectomy with upper vaginectomy have been reported for cervical carcinomas with promising fertility results. Only a few cases with fertility sparing surgery have been reported for the vaginal clear cell carcinomas. There is no reported pregnancy after radical abdominal trachelectomy upper vaginectomy and pelvic lymphadenectomy for vaginal clear cell carcinoma according to our knowledge. So here we present the case having pregnancy and disease free for 43 months after fertility sparing surgery due to vaginal clear cell adenocarcinoma.

Case: A 24 year-old woman underwent radical abdominal trachelectomy, pelvic lymphadenectomy and upper vaginectomy because of vaginal clear cell carcinoma before 43 months has a pregnancy at 28 weeks. Her pregnancy is normal and no evidence of disease. She had spontaneous pregnancy.

Conclusion: Pregnancy after fertility sparing surgery for vaginal clear cell carcinoma is possible without any other treatment for fertility.
Poster Session II

HPV DNA LOAD IS PROGNOSTIC FACTOR FOR VAIN DEVELOPMENT AFTER HYSTERECTOMY ESPECIALLY THAT WITHOUT CERVICAL LESION

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¹Obstetrics & Gynecology, Korea University Guro Hospital, ²Obstetrics & Gynecology, Korea University Anam Hospital, ³Obstetrics & Gynecology, Korea University Ansan Hospital, Seoul, Republic of Korea

Objective: This study will consider contributing factors of the VAIN development after hysterectomy with or without cervical lesion and it can help to evaluation for VAIN after hysterectomy.

Materials and methods: Between January 2000 and March 2011, we retrospectively reviewed the medical records of patients with VAIN after hysterectomy at the Department of Obstetrics & Gynecology, Korea University College of Medicine, Guro Hospital, Seoul, Korea.

Results: Forty three women were histologically confirmed VAIN by colposcopy guided biopsy. The mean age at diagnosis of VAIN was 56.7 years (range, 43-75). The mean period for the diagnosis of VAIN following hysterectomy was 61.9 months (range, 3-182). Twenty seven patients underwent hysterectomy with cervical lesion; 8 cases of cervical dysplasia, 19 cases of early stage cervical cancer (13; CIS, 4; stage Ia1, 2; stage Ia2). Sixteen patients underwent hysterectomy without cervical lesion. In previously hysterectomized women without cervical lesion has significantly high HPV DNA load (p=0.027) and high grade of VAIN (p=0.04). The age, parity, vaginal cytology, and period until the diagnosis of VAIN were not significantly different between two groups. Twenty-five patients were tested for HPV DNA load in two years after hysterectomy. There was a negative correlation of HPV DNA load and period until the diagnosis of VAIN (r=-0.736, p=0.000).

Conclusion: Development of VAIN after hysterectomy without cervical lesion is associated with higher HPV loads and more severe lesions than that with cervical lesion. Further studies are needed to clarify the pathogenesis of VAIN on the point of HPV replication.
Poster Session II

TREATMENT OF VULVAR INTRAEPITHELIAL NEOPLASIA - LASERABLATION OR SURGICAL RESECTION?

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Background: Vulvar intraepithelial neoplasia (VIN) is an increasing problem in women in their 40s. It is associated with carcinogenic HPV-infection, mostly type 16 and 18, smoking and immunocompromised status. The incidence in Denmark is 2,1/100,000 women. 3-4% of women with VIN experience progression to invasive cancer. The standard methods of treatment in Denmark are laserablation or surgical intervention.

Aim: To calculate the rate of recurrence after laserevaporation and surgery in our institution

Methods: Review of journal files for women diagnosed with VIN I-III and treated with either laserablation or surgery at Department of Obstetrics and Gynaecology, Odense University Hospital, Denmark, from 2009-2011.

Results: 68 women aged 22-83 were diagnosed with VIN I-III. 44 women had laserablation. 32 (72%) of these developed recurrence in the follow-up period, and 9 proceeded to a more severe state of VIN. 24 women had surgical treatment, 10 (41%) of these had recurrent disease and 4 proceeded to a more severe state of VIN. One patient developed invasive cancer. She had had both surgical treatment and laserablation. The choice of treatment depended on doctors' and patients' preferences.

Conclusion: VIN I-III can be treated with laserablation or surgery but both methods carries a considerable risk of recurrence and even progression. In our population there is statistically significant difference in the recurrence rate after laserablation (72%) compared to surgical resection (41%) (p = 0.02). Both methods must be succeeded by carefully follow-up. The lower recurrence rate after surgical resection must be taken into account when counseling the patients.
Poster Session II

PROGNOSTIC FACTORS IN VULVAR SQUAMOUS CELL CARCINOMA: VALUE OF NEW 2009 FIGO STAGING SYSTEM

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¹Department of Surgical Oncology, ²Department of Pathology, Medical University of Gdańsk, Gdansk, Poland

Objective: In 2009, FIGO modified staging of vulvar cancer - the prognostic significance of the new classification relative to the prior system as well as to commonly recognized prognostic factors has not been assessed. The aim of this study was to test prognostic ability of 2009 staging in a cohort of uniformly treated and staged cases with long-term follow up.

Methods: Pathologic characteristics were obtained by blind review of the original tissue samples. 76 patients qualified for surgery on the basis of the same criteria, with full clinical history were included in the study. The histological analyses were performed on 76 and 35 paraffin-embedded tissue samples from primary tumours and lymph nodes, respectively. Survival analyses included the Kaplan-Meier method, log-rank test, and Cox proportional hazards model.

RESULTS: Univariate analysis has demonstrated that age (p=0.0170), lymph node metastasis (p=0.0393), tumor grade (p=0.0086) and FIGO1994 stage (p=0.001) were significant prognostic factors for overall survival. Multivariate analysis has demonstrated that growing age (HR=2.25, 95%CI=0.79-3.71, p=0.0321), tumor grade (G1 vs. G2 and G3) (HR=1.31, 95%CI=1.6-4.62, p=0.0057) and FIGO1994 stage (HR=1.78, 95%CI=0.55-3.01, p=0.0061) are independent prognostic factors with respect to overall survival.

<table>
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<th>95% Confidence interval</th>
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<td>Positive</td>
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[Univariate analysis of prognostic variables in vul]

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</table>

[Multivariate analysis of prognostic variables in vul]
Conclusions: The results indicate the prognostic advantage of the 1994 FIGO staging as it has become an independent prognostic factor in contrast to the new FIGO system. This should be tested in future larger cohort studies. Differentiation grade turned out to be a very valuable independent prognostic factor and should be incorporated as a routine component of the histopathologic reports in vSCC.
Poster Session II

MAGEA-4 EXPRESSION IS INVERSELY CORRELATED WITH KI67 LABELING INDEX WITHIN PRIMARY TUMOR IN NON-METASTATIC VSCC PATIENTS

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1Department of Surgical Oncology, 2Department of Gynaecology, Gynaecological Oncology and Gynaecological Endocrinology, 3Department of Pathology, Medical University of Gdansk, Gdansk, Poland

Objectives: Previously we found positive correlation between MAGE-A4 expression and overall survival in non-metastatic vSCC cases. This novel correlation suggests that MAGE-A4 may belong to a group of tumor suppressor proteins. We hypothesized that MAGE-A4 exerts an anti-proliferative effect by mechanism associated with differentiation of cancer cells or apoptosis. The aim of this study was to analyze Ki67 labeling index (marker of proliferation) and caspase-3 (marker of apoptosis) within primary tumors derived from non-metastatic cases and to assess the correlation of both markers with the previously evaluated MAGEA-4 expression as well as with the overall survival.

Methods: Biopsy specimens from 45 non-metastatic patients with vSCC were examined for Ki67Li and caspase-3 expression by immunohistochemistry. The Ki67 labeling index was defined as percentage of immunoreactive tumor cells in the evaluated cancer nest. High score method was used for semiquantitative evaluation of caspase-3 expression. Data on MAGE-A4 were available for each primary tumor.

Results: Ki67Li and caspase-3 expression were not correlated with the overall survival among patients with local disease. Ki67Li was inversely correlated to MAGE-A4 expression (r=−0.354, p=0.023). Caspase-3 was not correlated to MAGE-A4 expression (r=−0.304, p=0.063) in this cohort.

Conclusion: Lack of prognostic significance of Ki67 labeling index and caspase-3 expression was notified in non-metastatic vSCC. Correlation between tumor MAGE-A4 expression and longer OS among these patients could be explained by the anti-proliferative effect of unknown mechanism, since MAGE-A4 showed inverse correlation to Ki67Li.
Poster Session II

INTRAEPITHELIAL GRB+ AND CD56+ INFILTRATES WITHIN PRIMARY VSCC TUMOR ARE CORRELATED WITH LONGER OS IN NON-METASTATIC AND METASTATIC CASES RESPECTIVELY

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Department of Surgical Oncology, Medical University of Gdansk, Gdansk, Poland

Objective: Previously we have found that adaptive immune response does not influence the patient prognosis in vSCC, therefore purpose of this study was to clarify the prognostic role of innate immunity represented by tumor infiltrates of CD56+ cells as well as granzyme B depended cytotoxicity estimated by granzyme B positive (GrB+) cells infiltrating cancer nests.

Methods: 76 primary tumors and 35 lymph node metastases derived from 76 patients with full clinical history were analysed. The infiltration of GrB+ and CD56+ cells within cancer nests were evaluated by immunohistochemistry and the correlation between the 2 was assessed. GrB+ and CD56+ infiltrates were compared with commonly recognized prognostic factors. The chief aspect analyzed was the overall survival.

Results: Only intraepithelial (ite) infiltration of immune cells was analyzed. The number of (ite) GrB+ cells within primary tumor was inversely correlated with age (r=-0.333, p=0.004), and correlated with tumor grade (r=0.304, p=0.009), while intensity of (ite) CD56+ cells at primary site was correlated with depth of invasion (r=0.339, p=0.003) and recurrence (r=0.295, p=0.011).

(ite) GrB+ cells were significantly related to (ite) CD56+ cells (r=0.386 p=0.017) in non-metastatic cases as well as high (ite) GrB+ infiltrates predicted longer OS among these patients (p=0.028). High (ite) CD56+ infiltrates were correlated with longer OS in metastatic cases (p=0.0019).

Conclusion: (ite) GrB+ infiltrates indicating cytotoxic function of innate and adaptive immune effectors predict longer OS among non-metastatic vSCC cases. The suggested protective role of (ite) CD56+ infiltrates at primary site in metastatic cases is probably not related to cytotoxic function of these cells.
CORRELATION BETWEEN CD44 ADHESION MOLECULE EXPRESSION AND LYMPH NODE METASTASIS IN VULVAR SCC: IS IT PREDICTIVE SIGNIFICANCE?

J.J. Sznurkowski¹, J. Kobierski², A. Zawrocki³

¹Department of Surgical Oncology, ²Department of Gynaecology, Gynaecological Oncology and Gynaecological Endocrinology, ³Department of Pathology, Medical University of Gdansk, Gdansk, Poland

Objectives: The aim of this study was to evaluate the expression of CD44 adhesion molecule in vulvar squamous cell carcinoma (vSCC), since an inappropriate expression of adhesion molecules could raise the metastatic ability of the tumor cells.

Methods: Biopsy specimens from 76 patients with vSCC were examined for the expression of CD44 by immunohistochemistry. The relationship of immunoreactivity with pathological features of the primary tumor and inguino-femoral lymph node metastasis were then analyzed.

Results: The CD44 expression was correlated with pT 2009 (r=0.263, p=0.024), but not correlated with tumor size (r=0.154, p=0.197), tumor grade (3 tier scale GOG) (r=-0.112, p=0.344) and depth of invasion (r=-0.044, p=0.710).

The correlation between CD44 expression within primary tumor and corresponding lymph node metastasis was not observed (r=-0.134, p=0.257).

23 patients (31.1%) had negative staining for CD44. Inguino-femoral lymph node metastasis was not associated with negative staining for CD44 (p=0.452). There was no difference in OS between CD44-negative and positive cases (p=0.379), as well as CD44 expression was not correlated to OS in the analyzed cohort of vSCC cases (0.306).

Conclusion: Our study reveals that reduced expression of CD44 should not be an indicator of high invasiveness of vSCC tumor cells.
Poster Session II

Typing of Human Papillomavirus (HPV) From Female Genital Warts

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Objectives: To describe the demographic features of female patients with genital warts, the characteristics of genital warts presented, treatment modalities used and to determine the type of HPV associated with the warts.

Methods: Prospective observational study on female patients with genital warts referred to Colposcopy Clinic of Groote Schuur Hospital, Cape Town from April to September 2010.

Results: 156 women were included. The median age was 27 years (Range 15-53). 94 (60.3\%) were new cases, 40 (25.6\%) had recurrent and 22 (14.1\%) had persistent disease. 123 (78.8\%) patients were HIV-positive and 83 (67.5\%) were on anti-retroviral treatment with a mean CD4 count of 338.72 cells/microl (Range 40-676). Treatment modalities included ablation with topical agents, cauterization and carbon dioxide laser. Two patients were diagnosed with vulva malignancy. In 33 (21.2\%) cases, the warts recurred within three months after treatment of which 28 (84.8\%) were HIV-positive. 119 (76.3\%) women were HPV DNA positive using Roche Linear Array Genotyping Test for high and low-risk types of HPV. Only 9 (7.6\%) patients with HPV DNA positive did not have either HPV 6 or 11 isolated. Among HIV-positive women, 96 (78.0\%) were HPV DNA positive and 43 (44.8\%) were infected with more than one HPV type, with the maximum number of types being 15 in one patient. 19 of 29 (65.6\%) HIV-negative women were HPV DNA positive and 3 (10.3\%) had more than one HPV type, with a maximum of 3 types recorded. The commonest HPV types in order of frequency in HIV-positive women were 11, 6, 89, 61, 55 and 62, and in HIV-negative women were 11 and 6.

Conclusions: Majority of the patients were HIV-positive. Warts recurred more commonly in HIV-positive patients following treatment. The commonest types of HPV isolated were 11 and 6 but types 89, 61 and 55 are emerging.
COMBINED EXTERNAL BEAM RADIOTHERAPY AND INTERSTITIAL BRACHYTHERAPY IN TREATMENT OF CANCER RECURRENCES AT THE EXTERNAL URETHRAL ORIFICE

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Purpose: Cancer recurrences at the external orifice after treating primary cancers of the cervix, vagina, and vulva are not easy to treat by surgery or EBRT because of complications. Combined EBRT and interstitial brachytherapy boost can increase dose to tumor, reserve the urethra, and keep tolerable dose to bladder and rectum. This study evaluates the feasibility of EBRT combined with interstitial brachytherapy in treatment of cancer recurrences at the external urethral orifice.

Methods and material: From April 2010 to April 2011, 3 squamous cell carcinomas recurred at the external urethral orifice (1 case after resection of vulva cancer, 2 cases after surgery of cervical cancer). Tumor size is 2-3 cm, 1 case had 2cm metastatic inguinal lymph node.

EBRT 50-60Gy/25-30 fractions/5-6 weeks was followed by interstitial HDR brachytherapy 15Gy/ 6 fractions/ 3 days. 1 catheter was attached to Foley catheter and inserted intra-urethrally. 2 catheters were inserted interstitially each side of the urethra 1-1.5cm from the urethra. In HDR brachytherapy treatment planning, dose was prescribed and normalized to 1cm from the tumor.

Results: All cases had complete response. Follow up until April 2012 (12-21 months after treatment), all cases had local control, no regional and distant metastasis. 1 case had sclerosis of the vulva (this patient had inguinal lymph node metastasis and received 60Gy EBRT). No case developed dysuria, hematuria, and late rectal complication.

Conclusions: Combined EBRT and interstitial brachytherapy can be used effectively in treatment of cancer recurrences at the external urethral orifice.
Poster Session II

TREATMENT OF VULVAR INTRAEPITHELIAL NEOPLASIA (VIN) WITH TOPICAL IMIQUIMOD 5% CREAM (ALDARA®): A RETROSPECTIVE CLINICAL STUDY

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Introduction: Commonly VIN is treated with ablative therapy often resulting in a loss of quality of life due to excision of vulvar tissue. Imiquimod activates Langerhans cells resulting in a TH1-dominant immune response that removes VIN without any long-term adverse events.

Objective: To assess the efficacy of imiquimod 5% cream for treating VIN according to grading, lesion size, appearance, distribution pattern, HPV-infection, age and coexisting lichen sclerosus.

Methods: 62 patients with biopsy proven VIN I-III were treated with imiquimod 5% cream in the Gynaecological Outpatient Department of the University Hospital of Freiburg between 2004 and 2011. Follow-ups ranged from 3 to 72 months (median 21 months).

Results: Complete response was observed in 47 of 62 (76%) women, partial response in 12 of 62 (19%) and weak partial response in 2 of 62 (3%) women. One patient did not respond. Recurrences occurred in 17 of 62 (27%) women. Recurrence rates were significantly lower in HPV-positive patients (p = 0.046). Fewer recurrences were observed in women under the age of 65 (p=0.030). Patients without signs of local inflammation under imiquimod treatment were significantly less likely to achieve complete response (p = 0.049). Response rates did not depend on lesion size. However, women with large lesions required longer treatment and higher total imiquimod dosage to achieve complete response.

Conclusion: Imiquimod 5% cream appears to be a favourable alternative to ablative treatment independent of grading, appearance and lesion size. Patient age, HPV status and occurrence of side effects had significant impact on treatment outcome.
Poster Session II

CLINICO-PATHOLOGICAL REVIEW OF EXTRAMAMMARY PAGET’S DISEASE (EMPD) OF VULVA IN A CHINESE POPULATION

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Background: EMPD is a rare vulvar neoplasm typically affecting Caucasian postmenopausal women. Information in Chinese population is scarce.

Aim: To study the characteristics of vulvar EMPD in Chinese women in a regional hospital in Hong Kong SAR.


Results: Seventeen Chinese women were identified (mean age 72, range 40-91). Majority (70.6%) complained pruritus. Mean time from symptom presentation to diagnosis was 52 months (range 2-96). Fifteen patients had cutaneous EMPD (11 intraepithelial, 4 adenocarcinoma). Wide local excision or vulvectomy was performed on 9 patients with intra-epithelial EMPD. Margins were microscopically involved in 4 patients. One received re-excision and none had recurrence. One of 5 patients with negative margin recurred at 15 months. Two patients with intra-epithelial EMPD were unfit for surgery, one had adjacent squamous cell carcinoma and died, the other progressed to adenocarcinoma 26 months later. One of 4 patients with adenocarcinoma was unfit for surgery. Three had radical vulvectomy and groin dissection. Negative margin was achieved in 1 case with no recurrence at 47 months. Two had positive margins, one recurred at 1 year with liver metastasis and one had no recurrence. Two patients had non-cutaneous EMPD. One with underlying urinary bladder malignancy and received palliative chemotherapy. The other patient with ano-rectal malignancy had abdominoperineal resection and vulval excision showed no disease recurrence at 24 months.

Conclusion: The clinico-pathological features and outcome of vulvar EMPD in Chinese population is similar to that reported in the literature.
Poster Session II

PRIMARY MALIGNANT MELANOMA OF THE VAGINA: A RETROSPECTIVE CLINICOPATHOLOGICAL STUDY OF 44 CASES
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Objective: Primary malignant melanoma of the vagina (PMMV) is an extremely rare, but highly aggressive tumor, with limited information regarding survival and prognostic factors. In order to identify prognostic predictors of survival and improve treatment selection, we performed this retrospective study.

Materials and methods: Between 12/2002 and 8/2011, 44 patients with histologically diagnosed PMMV in FUSCC were evaluated retrospectively. Prognostic variables were analyzed by both Kaplan-Meier survival analysis and Cox proportional hazards regression.

Results: The mean age of the patients was 58.7 years, and 77% of patients were postmenopausal women. Of the 44 patients, 41 were treated with surgery and 3 with radiochemotherapy only. The median follow-up time was 27.6 months (range, 3.0-94.3 months). Thirty (68.2%) of the 44 patients developed recurrences, and twenty-one (47.7%) patients died of disease. Median progression-free survival time was 14.4 months (95% confidence interval [CI]: 9.8-18.9 months) and median overall survival time was 39.5 months (95% CI 9.4-69.7 months). On multivariable analysis, depth of invasion was independent prognostic predictor for overall survival (P=0.041). Age, menopausal status, multifocal lesion, tumor size, the extent of surgery, adjuvant therapy, lymph node status and positive margin were all not statistically significant associated with PFS and OS, though lymph node status may have some tendency. And there was an obvious statistical association between depth of invasion and lymph node status (P=0.048).

Conclusion: Optimal treatment should be considered as surgery in favor of local wide excision for suitable women. The prognosis is influenced by depth of invasion and lymph nodes involvement.
Poster Session III

ARID1A STATUS DIVIDES THE MORPHOLOGICAL SUBTYPES OF OVARIAN CLEAR CELL CARCINOMA (CCC)

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Objective: To study the relation ARID1A expression to CCC molecular and pathological features.

Methods: 123 ovarian cancer samples; 56 of them were CCC, were immunohistochemically tested for ARID1A, HNF1β, ERα, P53, pAKT and Ki-67 after obtaining an informed consent from all patients.

mRNA expression microarray analyses was done for 14 CCC samples.

Results: 34 CCC cases showed negative ARID1A staining compared to other types which showed positive expression except for 4 cases. 75% of CCC cases showed positive HNF1β staining, while the other types gave reaction with only 4 cases. Expression of ERα is lost in 92.9% of CCC cases, while it is expressed in 72% of EAC and 50% of SAC.

ARID1A was correlated to HNF1β, ERα, P53 and Ki-67 but not with pAKT.

There is a significant difference in ARID1A expression between CCC morphological patterns, where the solid pattern showed higher ARID1A expression score than papillary pattern (p=0.0058).

Unsupervised hierarchical clustering of merged microarray data of our samples, GSE2109 and GSE6008 showed two major clusters, where ARID1A expression accumulated in one cluster.

Univariate and Multivariate analysis of the risk imposed by ARID1A on the Overall and Progression-free survival rates were not statistically significant.

Conclusions: This study shows that CCC has unique molecular features that differentiate it from other types.

HNF1β and PI3K pathways are activated while expressions of ARID1A and ERα are lost in CCC.

There are two subtypes of CCC based on ARID1A status which is related to CCC morphology.
Poster Session III

PROSPECTIVE FOLLOW-UP OF 2065 YOUNG UNSCREENED WOMEN TO STUDY HUMAN PAPILLOMAVIRUS INCIDENCE AND CLEARANCE

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Background: HPV is a necessary factor in the development of cervical cancer. However, HPV is a common sexually transmitted virus that is often cleared.

Objective: Analyze HPV type-specific incidence and clearance and its relation with age and sexual behavior in a group of young, unvaccinated, unscreened women.

Methods: 2065 women (18-29 years), were followed for 12 months and provided a 3-monthly self-collected cervico-vaginal sample and questionnaire. For HPV DNA detection the SPF₁₀⁻DEIA LiPΑ₂₅ system was used.

Results: Incidence rates of hr-HPV and lr-HPV were 17.0, and 14.3 per 1000-person months, respectively. HPV 16, 52, 51, and 31 had the highest incidence rates. Co-factors independently influencing HPV incidence were type of relationship, a new relationship, number of lifetime sex partners, frequency of sexual contacts, and condom use. The overall clearance of the newly detected hr-HPV, and lr-HPV infections was 61.2% and 69.0%, respectively. Having a sexual relationship and sexual age independently influenced the clearance of hr-HPV. Women with HPV 16 and a co-infection with another hr-HPV had a lower clearance rate than women only infected with HPV 16.

Conclusion: HPV incidence rates in this young Dutch study population are comparable to other western countries and not related to age. Independent factors significantly influencing incidence and clearance were all related to past or current sexual behavior. This relation with past sexual behavior forms a direct indication that viral latency exists, is rather common, and forms the challenge for future studies to distinguish true HPV incidence from detecting latent HPV.
Poster Session III

OUTCOME OF METASTATIC LYNCH SYNDROME-ASSOCIATED GYNECOLOGIC CANCERS

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Introduction: DNA mismatch repair is defective in Lynch syndrome associated cancers, but little data exists regarding their sensitivity to therapies that cause DNA damage. The objective of this study was to assess the response to treatment and survival of metastatic gynecologic cancers in women with Lynch syndrome.

Methods: Twenty-one patients (19 uterine, 1 ovarian, 1 fallopian tube) were identified from three institutions. Records were reviewed to determine patient characteristics, treatment and survival.

Results: Among 14 patients with primary advanced stage cancers, 7 had only nodal metastases and 7 had peritoneal and/or adnexal metastases. Adjuvant treatment included: chemotherapy and radiation (8), chemotherapy alone (5), radiation alone (1). Twelve of 14 patients (86%), including 7 with measurable disease after primary surgery, are alive without disease with a median survival of 69 months, and 10 of these patients are 5-year survivors. Among 7 patients treated for recurrent cancers, 2 had nodal metastases only and 5 had abdominal disease. Treatment included: chemotherapy and radiation (4), radiation alone (2), chemotherapy alone (1). Median survival was 57 months and 5/7 (71.4%) are alive without disease, including 5 patients who had measurable disease. Overall, 17/21 (81%) patients remain alive without disease.

Conclusions: Women with metastatic Lynch Syndrome-associated gynecologic cancers had a favorable response to therapy and were frequently long term survivors. These data suggest that, like BRCA1/2 associated ovarian cancers, metastatic gynecologic cancers that occur in women with Lynch Syndrome may also be highly sensitive to treatment with DNA damaging agents such as chemotherapy and radiation.
Poster Session III

METFORMIN DISPLAYS ANTI-PROLIFERATIVE ACTIVITIES IN ENDOMETRIAL CANCER CELLS VIA INTERACTION WITH THE IGF-IR SIGNALING AXIS

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Background: Studies have shown a correlation between obesity and endometrial cancer risk. Metformin is an anti-diabetes drug with potential anti-neoplastic actions. The aim of this study was to evaluate whether the antiproliferative actions of metformin are potentially mediated via suppression of the IGF-I receptor pathway.

Materials and methods: Human endometrioid Ishikawa and ECC (Type I) and serous (USPC-2 and USPC-1; Type II) endometrial cancer cell lines were treated with metformin (10 mM), in the presence or absence of IGF-I. The expression and activation of specific genes involved in IGF signaling was evaluated by Western blotting. Apoptosis was evaluated by cleavage of PARP, caspase-3, and Bcl2 measurements. Cell viability was measured by MTT assays.

Results: Metformin decreased the IGF-I stimulated phosphorylation of IGF-IR in ECC-1, USPC-1 and USPC-2 cells. Metformin up-regulated AKT and ERK1/2 phosphorylation in Ishikawa, ECC-1 and USPC-1 cells and down-regulated them in USPC-2 cells. Metformin down-regulated the expression of total IGF-IR and insulin receptor in USPC-1 cells and up-regulated IGF-IR levels in ECC-1 cells. In addition, the data showed that metformin induced a significant increase in cleaved PARP in USPC-1 and USPC-2 cells. Finally, MTT assays showed that metformin caused a decrease in proliferation rate compared with control cells.

Conclusions: In summary, our studies demonstrate that metformin displays potent apoptotic and anti-mitogenic actions in endometrial cancer cells that are mediated, at least partially, via interaction with the IGF-IR axis. Taken together, our results suggest that rational use of metformin may help reduce endometrial cancer risk.
Poster Session III

EVALUATION OF THE BIOLOGICAL ACTIONS OF INSULIN ANALOGUES IN ENDOMETRIAL CANCER CELL LINES

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Background: Modifications introduced into native insulin molecules may enhance their affinity for the IGF-I receptor (IGF-IR). The IGF-IR, which displays a close similarity to the insulin receptor (IR), has been correlated with a number of neoplastic processes. Endometrial cancer exhibits a significant association with obesity and diabetes. We hypothesized that insulin analogues may elicit atypical proliferative and signaling activities in endometrial cancer cells.

Methods: The ECC-1 and USPC-1 endometrial cancer cell lines were used in this study. Proliferative and anti-apoptotic effects of insulin analogues were determined by MTT assays and PARP measurements, respectively. The signaling pathways elicited by the analogues were assessed by Western blot.

Results: MTT assays revealed that insulin glargine increased proliferation rates in both cell lines. The proliferative response in ECC-1 cells displayed a dose-dependent curve whereas, in contrast, cells exposed to IGF-I and regular insulin reached plateau values. In addition, apoptosis measurements demonstrated that insulin glargine prevented PARP cleavage in USPC-1 cells. Furthermore, both insulin glargine and detemir were able to induce AKT and ERK phosphorylation in both endometrial cancer cell lines.

Conclusions: Our data indicate that long-acting insulin analogue glargine, but not detemir, exhibits IGF-I-like proliferative and anti-apoptotic effects in both endometrial cancer cell lines. Short-acting insulin analogues lispro and aspart exhibit enhanced proliferative activities only in ECC cells. Finally, insulin glargine and detemir elicit atypical signaling activities in both cell lines. The clinical implications of the biological actions of insulin analogues in endometrial cancer must be critically evaluated.
Poster Session III

GYNAECOLOGICAL CANCER CARE IN BRASILIA - BRAZIL. ROLE OF AN OPERATIONAL PUBLIC CARE REGIONAL REFFERENCE CENTRE UNDER CONSOLIDATION

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Introduction: Primary, secondary and tertiary care of gynaecological cancer patients in Brazil’s public health system is often regarded as non-supportive of patients’ with respect to timing of diagnostic results as well as surgical, adjuvant and palliative care. Upon establishing a regional reference centre for these patients in a central hospital we look forward to imprint a new flow of information and referral in order to make diagnostic and treatment procedures feasible concerning time, cost and effectiveness.

Objectives: To achieve our goals, a basic but reliable information system must be set in place, and the cornerstone is the statistical report of ambulatory and surgical procedures. We present the results of the first six months of survey.

Design: Observational study.

Methods: Data forms, statistical analysis with direct proportional calculations.

Results: 600 patients, main diagnosis were: Precancerous cervical lesions 300 (50 %), invasive cervical lesions 96 (18%), ovarian lesions (malignant and benign) 50 (8.33%), and endometrial / sarcomatous lesions 40 (6.67%). Mean age and range per diagnosed lesions: Precancerous cervical 41 (17 - 78), invasive cervical 49 (24 - 73), ovarian 41 (13 - 76) and endometrial / sarcomatous 62 (39 - 76). A total of 74 surgeries were performed, 10 of citoreductive/staging high complexity (12%), 22 (31%) of moderate and 42 (57%) of low complexity (Mainly conizations and LLETZ).

Conclusions: The high prevalence of precancerous cervical lesions and the high proportion of surgeries indicated for this diagnosis show need for continued work in cervical cancer prevention and reinforcement of the referral system.
Poster Session III

ASSESSMENT OF ETV5 AND RUNX1 EXPRESSION IN TYPE I ENDOMETRIAL CARCINOMA AND ITS ASSOCIATION WITH MYOMETRIAL INVASION

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Introduction: Endometrioid adenocarcinoma is the most common type of endometrial cancer: 80 to 90% of cases. Most of them are diagnosed in early stages and have a favorable prognosis, but some may present an unexpected recurrence, resistant to treatment. Prognosis is based solely on clinicopathological features, such as myometrial invasion. ETV5/ERM and RUNX1/AML1 expression present marked altered expression in stage IB endometrioid tumors. Therefore the purpose of this study was to evaluate the relation between ETV5/ERM and RUNX1/AML1 protein expression and myometrial invasion.

Material and methods: 169 patients with endometrioid adenocarcinoma underwent surgery at the Brazilian National Cancer Institute from 2007 to 2009. ETV5/ERM and RUNX1/AML1 protein expression was analyzed through immunohistochemistry (IHC) and evaluated as the percentage of IHC positive of tumors cells. Target and citrate antigen detection methods were applied to analyze immunostaining for ETV5. Tris-EDTA antigen detection was applied for RUNX1. RT-qPCR was applied for assessment of gene expression.

Results and discussion: ETV5 was expressed only in tumors (100%) whereas RUNX1 was expressed in normal (58.3%) and tumor tissue (100%). ETV5 presented both nuclear and cytoplasmic expression, whereas RUNX1 presented only nuclear expression (although in normal tissue it was expressed in cytoplasm). However, there was no difference in ETV5 or RUNX1 expression evaluation between stages IA and IB tumors. ETV5 expression was higher in 3+ IHC positive tumors, whereas RUNX1 expression was not correlated with IHC expression.

Conclusion: There is no association between ETV5 and RUNX1 expression and myometrial invasion in early stages of endometrioid adenocarcinomas.
Poster Session III

IDENTIFICATION OF TARGETED PROTEINS FOR ENDOMETRIOID ENDOMETRIAL CANCER

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Background and aims: Endometrial cancer is a common malignancy of the female genital tract with upring incidence and mortality in many countries. Endometrioid adenocarcinoma is the most common histology and is usual preceded by endometrial hyperplasia for years. To identify the potential risk of developing cancer in each woman with endometrial abnormality through a combination of histology and molecular markers might provide a way of cancer prevention through effective medical treatment for hyperplasia at risk.

Methods: Tissues of well preserved, early-staged endometrioid adenocarcinoma of endometrium from 5 patients were collected using laser capture microdissection. Normal endometrium glands in proliferative phase were microdissected for control. Proteomic approach to identify novel tumor-specific molecules was attempted by using LC-MS/MS and isobaric tags for relative and absolute quantification.

Results: 5,440 proteins were identified from cancer tissues. Of these identified 181 proteins were expressed > 2x, comparing to the control. These proteins are growth factors, proteins related to immune response, metabolic enzymes, calcium binding proteins, and proteins involved in regulating inflammation, proliferation and invasion. We then perform immunohistochemical staining to explore the expression of these proteins on achieved tissue microarray.
Intersection:
In cancer tissue, proteins were expressed > 2x, comparing to the control.

[Number of identified proteins in one or more iterations]
Distribution of protein according to their function classed by Ingenuity Pathway Analysis (IPA)
Conclusion: Our analysis led to the identification of novel molecular targets with the potential of molecular diagnosis of endometrioid carcinoma of the endometrium. Further study is warranted for the clinical usage of selected molecules as a diagnostic measure which might offer a less invasive, alternative diagnostic tool other than traditional dilatation and curettage.
Poster Session III

EVALUATION OF PROGNOSTIC SIGNIFICANCE AND FUNCTIONAL ANALYSIS OF ANDROGEN RECEPTOR CAG REPEAT POLYMORPHISM IN ENDOMETRIAL CANCER

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Introduction: Endometrial cancer (EC) is one of the most common gynecologic cancers in the world, and is a steroid hormone-related disease. Both epidemiologic and clinical studies have suggested that androgen and its intracellular receptor, androgen receptor (AR), are involved in EC. AR gene contains a CAG repeat (encoding for polyglutamine), highly polymorphic in length, that influences its transactivation function. A linear increase in CAG repeat length is associated with a progressive decrease in AR activity.

Methods: We have genotyped CAG polymorphisms of the AR gene in genomic DNA from a series of 72 consecutive patients with EC, and analyzed the results with regard to the characteristics and clinical outcome of patients. We categorized the CAG repeat lengths into 4 groups according to the quartile in our series, < 20, 20-21, 22-23, and >23.

Results: Our preliminary data found that shorter AR CAG repeat length is associated with poor disease-free survival and overall survival in EC patients. Cox regression also showed that patients with a shorter AR CAG repeat length had a shorter time to progression and worse overall survival when analyzed in the quartile or in the per unit increase of repeat number (hazard ratios (HR) 0.85, 95% confidence interval (CI) 0.76-0.96, P-trend = 0.006 for DFS; HR 0.82, 95% CI 0.73-0.93, P-trend < 0.001 for OS ;).

Conclusion: This study will not only discover prognostic biomarkers to improve the prediction of EC prognosis, but also help us understand the etiology of EC progression.
Poster Session III

SALINOMYCIN INHIBITS AKT/NF-KB AND INDUCES APOPTOSIS IN CISPLATIN RESISTANT OVARIAN CANCER CELLS


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Objective: Salinomycin is a monocarboxylic polyether antibiotic which is extensively used as coccidiostat in poultry and commonly fed to ruminant animals to improve feed efficiency. Recently, it has been shown to be highly effective in elimination of cancer stem cells both in vitro and vivo but molecular mechanism for its anticancer effect is not clear. The present study examined the effect of salinomycin to overcome cisplatin resistance in ovarian cancer. Inhibition of Akt/NF-κB is the first report in salinomycin-mediated apoptosis of cisplatin resistant ovarian cancer cells (A2780cp).

Methods: The cancer cells were cultured and treated with salinomycin. MTT assay was performed to determine cell viability. Flow cytometry and DNA fragmentation were performed to determine the effect on cell cycle and apoptosis. The expression of cell cycle regulatory-related proteins were evaluated by western blot analysis.

Results: The cell viability was significantly reduced by salinomycin treatment in a dose dependent manner. DNA fragmentation assay revealed apoptosis induction. Flow cytometry result showed that salinomycin induced sub-G1 arrest. Down regulation of Cdk2, Cdk4, up regulation of p27kip1 and concomitant increase in dephosphorylation of Rb were observed. Expression of survival protein Bcl-2 declined. Moreover, activation of caspase-3 and increased PARP cleavage triggered apoptosis. Salinomycin treatment reduced the Akt, pAkt and NF-κB levels. Up regulation of I-κBα further confirmed the NF-κB activation in this experiment.

Conclusion: Considering the importance of Akt/NF-κB signaling in cancer biology, the role of salinomycin may contribute to its toxicity towards cisplatin resistant ovarian cancer cells.
Poster Session III

PROFILING OF FIVE SERUM PROTEINS AFTER CHEMOTHERAPY PROVIDES ACCURATE ASSESSMENT OF THERAPEUTIC OUTCOMES AND SURVIVAL FOR OVARIAN CANCER


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Purpose: Despite advances in surgery and chemotherapy, advanced ovarian cancer is a lethal disease. The widely used CA125 is clearly not an effective biomarker for early stage cancer or for predicting therapeutic outcomes. Identification of novel biomarkers that can stratify prognosis may significantly improve patient care and their disease management.

Patients and methods: We profiled 46 serum proteins in 232 serum samples from healthy controls and 150 serum samples from ovarian cancer patients at three different disease stages: post diagnosis (PD), remission (RM) and recurrence (RC). The utility of these serum proteins as ovarian cancer biomarkers was evaluated using both univariate and multivariate models.

Results: Significant differences were found for 28 proteins in at least one of the three groups as compared to the healthy controls. We identified five proteins (sICAM1, sVCAM1, sgp130, sTNFR-II, and MMP2) that can significantly distinguish patient subset with poor overall survival than patients with better survival during remission both as individual markers and as a panel .( HR 18.41, p = 0.0003) (Figure 1)

[Figure 1]

Conclusion: A number of proteins, when tested after therapy and at the remission, have individually excellent prognostic value for overall survival of OC patients. If our results are validated, these biomarkers can be used to more accurately assess the therapeutic outcome for ovarian cancer.
Poster Session III

GYNECOLOGIC MALIGNANCIES WITH COEXISTING PELVIC TUBERCULOSIS. REPORT OF 7 CASES

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Background: Case series of gynecologic cancers coexisting with pelvic tuberculosis are being reported for their rarity. The aim of this paper is to share our experience with gynecologic cancers especially with primary fallopian tube carcinoma and to indicate a possible association between this tumor and tuberculosis.

Methods: 7 patients which were treated at the Gynecologic Oncology Department of Zekai Tahir Burak Women’s Health Education and Research Hospital with gynecologic cancers coexisting with pelvic tuberculosis are reviewed.

Results: Of the seven women reported, two were primary fallopian tube carcinoma, two were endometrium carcinoma, one was ovarian carcinoma, one was uterine leiomyosarcoma and one was malignant mixed mullerian tumor simultaneously occurring with pelvic tuberculosis. Mean age was 57.5 years. In two cases with fallopian tube carcinoma, tuberculosis salpingitis was demonstrated in the contralateral tube. All of the subjects except the one with primary fallopian tube carcinoma had elevated Ca-125 values.

Conclusion: There are only a few reports in the literature of gynecologic tumors co-existing with pelvic tuberculosis. Their rarity merits a report of every case. Medical awareness of peritoneal tuberculosis in the differential diagnosis of gynecologic malignancy is still lacking, especially in developing countries as tuberculosis may mimic malignant pelvic masses. In addition in developing countries, gynecologic malignant tumors with co-existing pelvic tuberculosis should always be kept in mind.
Poster Session III

SYNCHRONOUS PRIMARY TUMORS OF THE FEMALE GENITAL TRACT: A SINGLE CENTER EXPERIENCE OF 12 YEARS

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Objective: The present report aims to characterize the women diagnosed with synchronous primary malign gynecological tumors with emphasis on risk factors and synchronicity status. We also aimed to share our experience in such rare circumstance.

Methods: A total of 39 patients were identified with synchronous primary malign gynecological tumors between 2000 and 2012. Demographic, clinical and pathologic data were obtained from medical records and pathology reports.

Results: Mean age was 52.89 years. The majority of the study population (58.9%) was diagnosed with independent primary endometrial and ovarian tumors with 23 women. 8 patients were diagnosed with synchronous ovarian and cervical tumors, 4 women with independent cervical and endometrial tumors with different histological type, 3 women with ovarian and tubal tumors and one woman with ovarian cancer and uterine leiomyosarcoma. One woman with endometrial-ovarian tumor had also cervix carcinoma in situ. Diabetes mellitus and hypertension were significantly more common in women with endometrial-ovarian tumors. The most common presenting symptoms were pelvic/abdominal pain and abnormal vaginal bleeding.

Conclusion: Concurrent endometrial-ovarian tumors seem to occur in relatively older, overweight, multiparous and postmenopausal women with either diabetes mellitus and hypertension, while concurrent cervical ovarian-tumors are usually diagnosed in younger and leaner women who smoke.
THE FLAVONE BAICALEIN INHIBITS PLATINUM-RESISTANT EPITHELIAL OVARIAN CANCER CELLS AND INCREASES DDIT4 EXPRESSION

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Introduction: Platinum-based chemotherapy is commonly used to treat epithelial ovarian cancer. Unfortunately, patients often become resistant with few treatment options. Clearly alternative treatments are needed. We have identified a natural flavone, baicalein, which markedly upregulates DNA Damage Induced Transcript 4 (DDIT4) and suppresses cancer cell growth. We examined the activity of baicalein in ovarian cancer cells.

Methods: The ovarian cancer cell line A2780 and the derivative platinum resistant cell line A2780R were treated with baicalein or carboplatin, and growth was assessed at 72h by MTT assay. Alternatively cells were treated for 24h and quantitative RT-PCR was performed for DDIT4 expression.

Results: Baicalein and carboplatin similarly inhibited the growth of A2780 (Figure 1). However, in platinum resistant A2780R, baicalein continued to demonstrate growth inhibition while carboplatin was completely ineffective at the same concentrations. DDIT4 expression increased in a dose dependent fashion in both cell lines treated with baicalein (Figure 2). In contrast, DDIT4 expression was not altered in carboplatin-treated A2780R cells, where as A2780 cells displayed increased DDIT4 expression.
Figure 1

A2780 - Baicalein vs Carboplatin

A2780R - Baicalein vs Carboplatin

[Figure 1]
Conclusions: Baicalein can inhibit growth of platinum sensitive and resistant ovarian cancer cells. The inhibitory effects of baicalein correlate with DDIT4 expression. Baicalein may be a novel treatment option for ovarian cancer, especially platinum resistant cancer. DDIT4 appears to correlate with growth inhibition which may make its expression useful as a biomarker of response for both baicalein and carboplatin treatment.
Poster Session III

SEROUS OVARIAN CANCER PATIENTS HAVE LOWER LEVELS OF IgM ANTIBODIES TO VARIOUS GLYCANS COMPARED TO HEALTHY WOMEN

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Changes in glycosylation commonly occur in ovarian cancers. Such modifications can impact on the patient's humoral immune response; hence affect the anti-glycan antibody (AGA) profile of plasma and ascites.

Compare the AGA profile of serous cancer patients with healthy women to identify novel biomarkers of the disease. Investigate the biological function of various glycans identified to be of interest.

Plasma and ascites were collected from 11 patients with stage III or IV serous cancers and 14 healthy controls. A custom-made printed glycan array (PGA) allowed the simultaneous detection of AGAs to 203 chemically synthesised glycans, including some known tumour-associated carbohydrate antigens.

Antibodies to a broad spectrum of glycans were detected in both plasma and ascites by PGA. Serous cancer patients and controls have significantly different levels of plasma IgM to 31 glycans, where IgM levels were invariably lower in the cancer group. Significant differences in plasma levels of IgG to 4 glycans were also found. We validated these results using an in-house developed suspension array in independent cohort. From these studies, a number of glycans were identified to be of major interest such as P1 (Galα1-4Galβ1-4GlcNAc), neuraminic acid (Neu5Ac) and chitobiose (GlcNAc1-4GlcNAc). The human serous ovarian cancer cell line, IGROV1, was shown to express the trisaccharide P1. In vitro cell-based assays revealed that P1 expression correlated with faster tumour cell migration but slower proliferation. Anti-glycan antibodies have potential as biomarkers for ovarian cancer and are cohort independent. Targeting glycans which drive tumorigenesis may prove to have therapeutic potential.
THE ROLE OF IQGAP1 AND β-CATENIN IN OVARIAN CANCER PROGRESSION

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Ovarian cancer is associated with a poor prognosis and in advanced FIGO Stage with a 30% 5-year survival. Our aim was to examine candidate biomarkers for their diagnostic and therapeutic potential. Previously, we identified IQGAP1 as a marker of metastasis in glioma patients. IQGAP1 is involved in cellular adhesion, migration and angiogenesis, and in regulation of β-catenin mediated transcription. Dysregulated function of both proteins has been observed in various cancers, with IQGAP1 overexpression and decreased nuclear β-catenin levels associated with poor outcome. We hypothesised that in ovarian cancer, IQGAP1 and β-catenin expression and cellular localisation would correlate with disease progression and patient survival.

Immunohistochemistry (IHC) was employed to examine a cohort of 721 ovarian cancer patients and healthy controls for protein expression and cellular localisation of both IQGAP1 and activated β-catenin. Additionally, RT-qPCR and Western Blotting were used to screen a panel of ovarian cancer cell lines and primary cultures.

Over-expression of IQGAP1 was observed in metastatic lesions when compared to the matched primary tumour from the same individual. In cell lines, no significant alteration was observed at the mRNA or total protein level; however, increased plasma membrane expression of IQGAP1 was associated with the more aggressive serous subtype. A total absence of activated β-catenin expression in the nucleus was also observed for all normal and cancer cases.

This study indicates that IQGAP1 is a potential new marker for ovarian cancer progression and metastasis, and suggests that IQGAP1-targeted therapies may be useful for treatment of advanced ovarian cancers.
Poster Session III

SYNDECAN-1 AND HEPARANASE EXPRESSION IN OVARIAN CANCER: MODULATION AND POTENTIAL TARGETING

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Objective: Syndecan-1 (CD138) is a heparan sulfate (HS) proteoglycan expressed on several epithelial tumors. It plays a potential role in growth factor signaling, is implicated in cancer cell invasion and metastasis and has been used as a receptor for gene therapy in tumors. Heparanase is a HS-degrading enzyme that may also play an important role in tumor adhesion and spread. The mechanisms of interaction between Syndecan-1 and Heparanase are currently under study. This study investigates the effects of immunomodulators and environmental alterations on the expression of Syndecan-1 by ovarian cancer cells.

Methods: 5 Ovarian cancer cell lines were cultured in growth medium supplemented with varying concentrations of fetal calf serum (FCS), in the presence and absence of 17-β-estradiol, 5-azacytidine, valproic acid, trichostatin, interferon (IFN) and phorbolester. FACS analysis was performed after 48-72 hours of exposure to quantify Syndecan-1 expression. Heparanase activity was measured by incubating radioactive HS with cell lysates and separating the resulting fragments by size.

Results: Syndecan-1 was expressed by the majority of cells (50-98%) in all cell lines investigated. Heparanase activity was apparent in several. Estrogen and 5-azacytidine had no effect on Syndecan-1 expression. However, HDAIs, IFN and phorbolester suppressed Syndecan-1 significantly.

Conclusion: Syndecan-1 is expressed by a large subpopulation of ovarian cancer cells whereas Heparanase shows inconsistent activity. These molecules’ roles in growth factor signaling, proliferation, invasion and metastases make them interesting candidates for targeted therapy. Syndecan-1 expression on ovarian carcinoma cells is suppressed by HDAIs, phorbolester and IFN, and is sensitive to microenvironmental conditions.
Poster Session III

WEIGHT LOSS AND VISFATIN REDUCTION AS A BREAST CANCER RISK FACTOR

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Background and aims: The relationship between obesity and cancer made a lot of interest. Obesity has an important role in the etiology of breast cancer. Adipocytokines, secreted from adipose tissue have a strong link with breast cancer development. Visfatin is a novel adipokine which its increased expression has been shown in human breast cancer cells. On the other hand, increased visfatin secretion is associated with increasing total body fat mass. The purpose of this study was to investigate the changes of visfatin after weight loss and the association of these changes with anthropometric parameters in morbidly obese subjects following restrictive bariatric surgery.

Methods: 25 severely obese women were studied prior to and 1 month after bariatric surgery aged 35±9.4yr. BMI, waist circumference, waist to hip ratio and visfatin, were measured. Data were compared between groups by using t-test. P values < 0.05 was considered as a significant.

Results: Patients lost 12.2±4.3% of the initial body weight. Serum visfatin levels decreased from 5.1±3.7 to 3.3±3.1 ng/ml (P < 0.048). BMI reduced from 44.4±4.2 to 39±4.5 kg/m², waist circumference decreased from 119.4±10.7 to 107.8±9.4cm (P = 0.000) and also waist to hip ratio decreased significantly from 0.88±0.08 to 0.84±0.06.

Conclusion: Weight reduction 1 month after bariatric surgery was associated with a significant reduction in circulating visfatin levels in morbidly obese subjects and these changes may have protective effects against the risk of breast cancer among morbidly obese women.
EX VIVO EXPANSION OF CYTOKINE-INDUCED KILLER CELLS FROM OVARIAN CANCER PATIENTS IS ENHANCED BY IL-7 WITHOUT PROMOTING SUPPRESSOR ACTIVITY

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Objective: Interleukin (IL)-7 plays dual roles in T-cell maturation, proliferation, and activation. It promotes maintenance of immunosuppressive T-regulatory cells (Tregs), but also enhances proliferation of effector T-cells. Herein, we compared the cytotoxic response elicited by cytokine-induced killer cells (CIK) expanded from ovarian cancer (OC) patients in the presence or absence of IL-7.

Methods: Peripheral blood mononuclear cells (PBMC) isolated from OC patients (n=5) were expanded in a cocktail of IL-2, IL-12, and anti-CD3 antibody with or without IL-7. Ex vivo expanded CIK were co-cultured with an OC cell line (SKOV3-AF2) with IL-2 and/or interferon (IFN)α-2b to determine cytotoxicity elicited by CIK.

Results: CIK expanded exponentially under both culture conditions over approximately three weeks; however, the average fold expansion was doubled in the presence of IL-7 (132-fold) compared to cultures without IL-7 (68-fold). Expansion cultures consisted primarily of T-cells (>98%) by days 7-8. CIK expanded under both culture conditions elicited a significant cytotoxic response against SKOV3-AF2. However, no significant difference (p=0.76) was observed in cytotoxicity elicited against SKOV3-AF2 cells by CIK expanded in IL-7 (25.6%) compared to CIK expanded without IL-7 (27.8%). Cytotoxicity was CIK-dependant as there was no significant response in the negative controls lacking CIK cells (0.6%).

Conclusions: IL-7 enhanced ex vivo expansion of CIK from OC patients. Data demonstrates that addition of IL-7 does not promote Treg suppressor activity during ex vivo expansion. Addition of IL-7 may be helpful with increasing the number of CIK for cellular therapy protocols without any significant decrease in cytotoxic effect.
IMPACT OF VIRAL HEPATITIS B (HBV) ON CERVICAL HUMAN PIPILLOMAVIRUS (HPV) INFECTION

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**Background:** HPV and HBV share clinical similarities, only small proportion failure to eradicate virus can lead to chronic infection and cervical and liver cancer development.

**Objective:** To investigate HBV and HPV association.

**Methods:** A cross-sectional study was conducted in 3,717 HPV unvaccinated Thai women, aged 20-70 years, mean 45 years, at Chulabhorn Hospital, Bangkok, Thailand during July 19, 2011-April 3, 2012. HPV genotyping (Linear array, Roche, USA) and liquid-based cytology (Surepath, Becton and Beckinson, USA) were utilized. Blood testing for HIV, HBsAg, and VDRL was performed. Residual liquid based cytology solution was implemented for *Chlamydia Trachomatis* (CT) and *Neisseria Gonorrhea* (NG) by Cobas 4800 CT/NG test (Roche, USA). Candida was defined by cytological diagnosis.

**Results:** 36 females were excluded. The HPV prevalence was 15.5%, with 7.1% high risk (HR)HPV, 9.8% low risk (LR)HPV, and 1.6% probable HR. The positive results for HIV, VDRL, HBsAg, CT, NG, candida were 0.2%, 1.7%, 6.9%, 1.2%, 0%, and 7.5%, respectively. Univariated analysis revealed odd ratio (OR) (95%CI, p-value) for HPV infection in HIV, VDRL, HBsAg, CT, candida positivity was 5.49(1.11-27.27, 0.03), 0.81(0.38-1.71, 0.58), 0.66(0.44-0.99, 0.04), 5.92(3.23-10.83, < 0.001), and 1.30(0.95-1.79, 0.10), subsequently. NG could not be analyzed and no event was found. Using multivariated analysis, HIV and CT were still predictive factors for HPV, but HBV had negative effect on HPV. For HR-HPV association, only CT infection had significant positive correlation. For HBV/HR-HPV relation OR was 0.57 (95%CI=0.28-1.06, p=0.08).

**Conclusion:** HBV positive women had a lower risk of HPV infection.
Poster Session III

A PHASE I CLINICAL TRIAL OF THE SEROTYPE-CHIMERIC, INFECTIVITY-ENHANCED CONDITIONALLY-REPLICATIVE ADENOVIRUS (CRAD), AD5/3-Δ24, IN PATIENTS WITH RECURRENT GYNECOLOGIC CANCER


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Objective: Ad5/3-Δ24 has a type-3 knob incorporated into the type-5 fiber of this CRAd. This modification has demonstrated enhanced ovarian cancer infectivity. Preclinical studies have shown that Ad5/3-Δ24 achieves significant oncolysis and anti-tumor activity in ovarian cancer models. This study's purpose was to identify toxicities, MTD, efficacy, and biologic effects of intraperitoneal (IP) Ad5/3-Δ24 in select recurrent gynecologic cancers.

Methods: Eligible patients were treated with IP Ad5/3-Δ24 for 3 consecutive days in one of three dose cohorts ranging 1 x 109-1 x 1012 vp. Toxicity was assessed utilizing CTC grading and efficacy with RECIST. Ascites, serum, and other samples were obtained to evaluate gene transfer, generation of wild type virus, viral shedding, and antibody response.

Results: A total of 10 patients were enrolled. One patient encountered a complication with IP catheter placement, and did not receive treatment. The remaining 9 patients completed Ad5/3-Δ24 treatment protocol. A total of 15 vector-related AEs were experienced in 5 patients; all were grade 1-2 in nature. The most common vector-related AE included fever. Of 8 patients evaluable for response, 6 patients had stable disease, 2 patients had progressive disease. One patient experienced progression, clinically deteriorating prior to study end. Three patients had decreased CA125 from pretreatment levels one month after treatment; one of these patients normalized her CA125. All patients experienced an anti-adenoviral neutralizing antibody effect. Ancillary biologic studies are pending.

Conclusions: This study demonstrates the feasibility and safety of the serotype chimeric infectivity-enhanced CRAad, Ad5/3-Δ24, as a potential therapeutic option for recurrent gynecologic cancer patients.
INCORPORATION OF A NOVEL DUAL IMAGING VIRAL TRANSFER AND REPLICATION MONITORING STRATEGY INTO VIROTHERAPY FOR OVARIAN CANCER

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Objectives: Our early-phase clinical trials have recently validated the potential efficacy of infectivity-enhanced conditionally replicative adenoviruses (CRAd) as novel virotherapeutic approaches for ovarian cancer. We report on our efforts to noninvasively assess gene transfer and viral replication via incorporation of dual imaging capacity in our infectivity-enhanced CRAd.

Methods: A PET-compatible imaging motif transgene, SSTR, and a direct bioluminescence imaging capsid protein, mCherry, were genetically incorporated into the serotype chimeric, infectivity-enhanced CRAd, Ad5/3Δ24. Genomic incorporation and stability of mCherry red fluorescent protein into the viral capsid was validated. Transgene expression and somatostatin binding capacity of the SSTR imaging motif were also verified. Replication and oncolysis were evaluated utilizing luciferase-reporting assay in SKOV3 cancer cells.

Results: SSTR transgene expression was confirmed via FACS in SKOV3ip1/Luc cells. Somatostatin binding was demonstrated with [¹²⁵I]-Tyr-11-SST-14 binding assay. Western blot confirmed incorporation of the pIX-infused mCherry fluorophore. MCherry expression analysis showed Ad5/3Δ24-pIX-mCherry-E3-SSTR2 achieved acceptable expression compared to other control vectors. Ad5/3Δ24-pIX-mCherry-E3-SSTR2 replication was confirmed in vitro. Compared to controls, luciferase assay assessment showed only a slightly reduced oncolytic effect in SKOV3ip1 cells exposed to Ad5/3Δ24-pIX-mCherry-E3-SSTR compared to controls. CRAd. Validation of dual imaging capacity in vivo is ongoing.

Conclusions: Ad5/3Δ24-pIX-mCherry-E3-SSTR2 appears to effectively embody novel dual imaging capacity without impairing replication or oncolysis. Further investigation appears warranted.
Poster Session III

EPGENETIC REGULATION OF SOCS EXPRESSION AND RADIORESPONSE MODULATION BY SOCS OVEREXPRESSION

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Objective: The objective of this study was to elucidate the mechanism of elevated radioresistance of SOCS-1, 3 overexpressing cervical cancer cells.

Methods: The cell lines including HeLa, CaSki, ME-180, SiHa were employed for the experiments. We established stable SOCS-overexpressing HeLa cell line with pLNCX2-mSOCS1-Myc and pLNCX2-mSOCS3-FLAG. The expression of SOCS gene were measured by realtime PCR. For epigenetic regulation experiment, Trichostatin A, interferon gamma, and oncostatin-M were applied to culture dishes to check the change of SOCS expression level through time interval. We also analysed the reactive oxygen species level in overexpressing HeLa cells with FACS. To compare the activation levels of associated signal molecules such as MAPKs, Akt, and Stat, western blot was performed.

Results: In the process of SOCS-1, 3 induction by IFN-gamma, there was no difference of expression as the level of DNA hypermethylation or histone acetylation. Oncostatin-M(OSM) induced SOCS-1, 3 with little difference in the aspect of DNA hypermethylation or histone acetylation status. We performed chromatin immunoprecipitation (ChIP) to investigate the association of histone acetylation and SOCS induction by INF gamma or OSM. For both SOCS-1 and 3, IFN gamma decreased histone acetylation in promoter region, while OSM increased histone acetylation three times. SOCS overexpressing cells showed similar thioredoxin level with wild type HeLa cells. In addition, ROS-related molecules such as CAT, NQO1, HO-1, and PRDX2 showed a little (30%) lower expressions. Both PI3K-Akt signaling system and MAPK signaling system showed little difference of activation between SOCS overexpressing cells and wild type HeLa.

Conclusion: SOCS overexpression induced p21 level and G2/M cell cycle arrest after irradiation, which could be an important mechanism of radioresistance.
Poster Session III

ANALYSIS OF CANCER STEM-LIKE CELLS FROM PRIMARY OVARIAN CANCER BY ALDEFLUOR ASSAY


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Background: Some subtypes of epithelial ovarian cancers (EOC) often show a comparatively good response to chemotherapy, but may recur within several years despite comprehensive anti-cancer therapies. Cancer stem-like cells (CSCs) are defined as cancer cells which have higher tumor-initiating ability, and are resistant to chemotherapy, thus CSCs are one of major mechanisms of cancer recurrence after treatment. In this presentation we isolated and analyzed CSCs from epithelial ovarian cancer cell lines and primary ovarian cancer tissues (tumor or ascites).

Methods and results: We isolated aldehyde dehydrogenase 1 (ALDH1)-positive cells from ovarian carcinoma cell lines (AMOC2, HUOA, OVCAR3, SkOV3, ES2, RMG-1, HMOA, MCAS, HTBOA) by ALDEFLUOR assay. The rates of ALDHbright (ALDHbr) cells from EOC cell lines (8 out of 9) were 3.5% to 21.8%. Higher tumor-initiating ability of ALDHbr cells was confirmed by xenograft transplantation into NOD/SCID mice, indicating that CSCs were enriched in ALDHbr population. Similar ALDHbr cells were detectable in primary ascites of ovarian carcinoma cases (3 out of 6 cases), and the ALDHbr rates were ranged from 2.5% to 8.3%, and the tumor-sphere forming ability was higher in ALDHbr cells.

Conclusion: These observations indicated that ALDEFLUOR assay is useful and promising approach to identify CSCs from EOC and the molecular mechanisms of EOC CSCs were under investigation.
Poster Session III

TGB-ß PROMOTE EPITHELIAL MESENCHYMAL TRANSITION IN OVARIAN CANCER SPHEROIDS

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Purpose: The purpose of this study was to investigate the roles of TGF-ß treatment associated with the induction of epithelial mesenchymal transition (EMT) in ovarian cancer spheroids and to compare EMT markers expression in paclitaxel resistant (PR) cell lines.

Methods: The human ovarian cancer cell line SKOV3 and OVCAR3 were exposed to increasing doses of paclitaxel and established stable cell lines resistant to paclitaxel. Increasing paclitaxel resistance of spheroid forming cells and PR cells were assessed by cell viability assay. After TGF-ß treatment in spheroids, western blot analysis and real time PCR were used to assess the status of E-cadherin, vimentin, matrix metalloproteinases (MMP) -2 and Snail in the spheroids and PR cells.

Results: The PR and spheroid cells showed phenotypic changes consistent with EMT. Both cells had decreased expression of E-cadherin, and an increase in the vimentin, MMP-2 and Snail. TGF-ß treatment caused more increased vimentin, MMP-2 and Snail activation in ovarian cancer spheroid cells compared to those in the PR cells.

Conclusions: TGF- ß may contribute to the EMT induction in chemo-resistant ovarian cancer cells. TGF- ß related pathway may be targeted for the therapeutic intervention of patients with paclitaxel resistant ovarian cancer.
Poster Session III

FREQUENT EPIGENETIC INACTIVATION OF THE NORE1 TUMOR SUPPRESSOR IN HUMAN CERVICAL CANCERS

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Objectives: NORE1 (RASSF5) is a newly described member of the RASSF family with Ras effector function. Expression of the NORE1 gene is frequently inactivated by aberrant promoter hypermethylation in some human primary cancers and tumor cell lines, suggesting that NORE1 might be a tumor suppressor in human cancers. However, expression and mutation status of NORE1 and its implication in human cervical tumorigenesis has not been evaluated.

Methods: To explore the possible implication of NORE1 inactivation in cervical carcinogenesis, we characterized the expression, mutation, and methylation status of NORE1A and NORE1B in 9 cancer cell lines and 60 primary tumors. Quantitative PCR, SSCP, and bisulfite DNA sequencing analyses was performed using the standard method. Effect of NORE1A and NORE1B expression on tumor cell growth was evaluated using cell number counting, flow cytometry, and colony formation assays.

Results: Expression of NORE1A and NORE1B transcript was easily detectable in all normal cervical epithelial tissues we examined, but substantially NORE1B decreased in 3 of 9 (33.3%) cancer cell lines and 13 of 60 (21.7%) primary tumor tissues. None of 60 primary tumor show abnormal reduction of NORE1A expression. Moreover, 10 matched tissue sets exhibited abnormal reduction of NORE1B expression. While allelic deletion or somatic mutations of the gene were not identified, NORE1B expression was re-activated in all low expressor cells after treatment with the demethylating agent 5-aza-dC, suggesting epigenetic inactivation of the gene in tumors. Bisulfite DNA sequencing analysis of 31 CpG sites within the proximal promoter region demonstrated that abnormal reduction of NORE1B transcript in cancer cell lines and primary tumors is tightly associated with aberrant promoter CpG sites hypermethylation.

Conclusion: Collectively, our data indicate that epigenetic inactivation of NORE1B due to promoter hypermethylation is a frequent event in cervical tumorigenesis and might be implicated in the malignant progression of cervical tumors.
Poster Session III

BIOMARKER DISCOVERY IN THE DIFFERENTIAL EXPRESSION PATTERNS BETWEEN EPITHELIAL LAYERS IN CERVICAL DYSPLASIA

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Normal human cervical squamous epithelium consists of a differentiating continuum of cell layers. It is hypothesized that the basal layer consists of stem cells and that as cells migrate towards the surface they mature and differentiate. Hence, cells in different layers of the epithelium are expected to express different genes. Carcinogenesis upsets this regulated process. We seek to explore the molecular basis of the carcinogenic process by studying differences in expression between cervical epithelial layers across various grades of cervical intraepithelial neoplasia (CIN), hopefully leading to better biomarkers for detecting CIN at highest risk of progression.

CIN biopsies were fixed in Tissue-Tek Xpress Molecular Fixative and embedded in paraffin (MFPE). These were microdissected to collect the top and bottom halves of epithelium separately. RNA was purified using the Qiagen RNeasy FFPE kit. mRNA was labelled using the Agilent Low Input Quick Amp Labeling kit and tested on the Agilent Whole Human Genome 4x44K Microarray.

We present data from several cases spanning benign tissue to CIN III. Some samples were analyzed in duplicate to assess experimental variability. The scatter observed in comparing duplicate samples established a threshold for differential expression between the epithelial layers. Potential targets will be validated by immunohistochemistry and results for some candidate cancer biomarkers will be presented. Expression profile analyses generally treat the epithelium as a homogeneous unit. This work demonstrates that analysis of different epithelial layers in MFPE samples is feasible and can identify genes whose altered spatial expression may play a role in cancer progression.
Poster Session III

LOW DOSE HISTONE DEACETYLASE INHIBITOR, LBH589, POTENTIATES ANTICANCER EFFECT OF DOCETAXEL IN EPITHELIAL OVARIAN CANCER VIA PI3K/AKT PATHWAY

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Aim: The objective in this study was to investigate the effect of combination of LBH589 with docetaxel (DTX) on the growth and survival of epithelial ovarian cancer (EOC) cells in vitro and the possible mechanisms of chemo-sensitization of LBH589 in the combination treatment.

Methods: The effect of LBH589 alone or in combination with DTX on four EOC cell lines was studied by MTT and clonogenic assays, acridine orange (AO)/ethidium bromide (EB) staining for apoptosis, Western blotting for apoptosis-related proteins, histone H3 and H4 proteins, DNA double strand break (DSB) repair marker and phosphorylation of Akt.

Results: LBH589 alone inhibited EOC cell proliferation in a time-and-dose-dependent manner. Low-dose of LBH589 (IC₂₀) combined with DTX had a synergistic effect and greatly improved efficacy of DTX cell killing in EOC cells. Compared to DTX alone, the combination treatment with LBH589 and DTX induced more apoptosis and led to an increased and persistent DSB. Cell death following single or combined treatment was associated with the release of cytochrome c activity, increased caspase-3 (active) and PARP-1(cleaved), histone acetylation-related proteins and PI3k/Akt signaling pathway.

Conclusions: We have demonstrated for the first time that LBH589 inhibited EOC cell proliferation in a dose-dependent manner and low-dose LBH589 combined with DTX greatly enhanced killing of EOC cells. The putative mechanisms of the synergistic effect of this combination treatment in EOC cells include induction of apoptosis and more DNA damage via PI3K/Akt signaling pathway. This combination treatment may offer opportunities for novel therapeutic strategies in EOC treatment.
Poster Session III

CYTOTOXIC EFFECT AND INDUCTION OF APOPTOSIS IN HUMAN CERVICAL CANCER CELLS BY ANTRODIA CAMPHORATA

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Introduction: Antrodia camphorata is a Chinese herb indigenous to Taiwan. Previous reports demonstrated that it could induce apoptosis in some cancer cells. In this study we investigate whether the crude extract of A. camphorata (CEAC) can induce apoptosis in cervical cancer cells and the possible mechanisms involved.

Methods: Two human cervical cancer cell lines, HeLa and C-33A, were treated with CEAC (10-1000 µg/ml). The cytotoxic effect was tested by MTT assay. Apoptosis-associated DNA fragmentation was determined using an ELISA method. Activities of caspase-3, -8, and -9 of the apoptotic pathways were examined by caspase activity assay. Western blot analysis was used to examine the expressions of cytochrome c and Bcl-2 family proteins.

Results: The MTT assay revealed that CEAC was cytotoxic to both the cervical cancer cells in a dose- and time-dependent manner. The oligonucleosomal formation from the cleaved chromosomal DNA increased 2.3- and 4.4-folds in Hela and C-33A cells, respectively, when they were treated with CEAC at 400 µg/ml. The activity of caspases and the cytosolic level of cytochrome c also increased significantly in a dose-dependent manner in these two cell lines after CEAC treatment. Altered expression of Bcl-2 family proteins was noted with increased Bim and Bad in both the cervical cancer cells. In addition, decreased expression of Bcl-xL and Bcl-2 in HeLa cell and decreased Bcl-xL in C-33A cell were also observed.

Conclusion: From the results of this in vitro study, we suggest that A. camphorata is cytotoxic to the cervical cancer cells through apoptosis. It could be a potential agent in treating cervical cancer.
Poster Session III

OVARIAN TUMOR MALIGNANCY RISK ASSESSMENT TOOL CONSISTING OF HE4, CA125, ULTRASONOGRAPHIC SCORE AND MENOPAUSAL STATUS

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A case-control study included 83 ovarian cancer patients, 77 patients with benign ovarian tumors and 82 healthy control subjects in the control group. Objective of the study is to analyze biomarker concentrations included in the two novel ovarian tumor differential diagnostic tests (ROMA and OVA1) approved by Food and Drug administration in patients with ovarian tumors and to establish a new ovarian cancer risk assessment algorithm in conjunction with ultrasound score and menopausal status.

Ovarian cancer diagnostic tests developed in the training setting were evaluated in the independent validation settings of Asian pacific Ovarian cancer biomarker research group study population and Denmark Pelvic Mass Project population.

Results: Mean serum concentrations of CA125, HE4 and beta-2-microglobulin were upregulated, but apolipoprotein A1, transferrin and transthyretin down-regulated among ovarian cancer patients. When only one biomarker was introduced in the logistic regression analysis together with ultrasonographic score and menopausal status, HE4 (AUC=0.930; 95% CI 0.891-0.969) was more accurate than CA125 (AUC=0.902; 95% CI 0.855-0.949) in ovarian cancer diagnostic. But when both biomarkers were included in the logistic regression analyses ovarian cancer diagnostic accuracy was increased (AUC=0.939; 95% CI 0.902-0.977).

Conclusions: Human epidydimis secretory protein 4 and CA125 in combination with ultrasonographic features and menopausal status had the highest accuracy in ovarian tumor differentiation, however, newly established diagnostic tool should be used only in situations where there are doubts about necessity of surgical intervention because of high surgical complication risk or severe co-morbidities and in cases with clinical suspectability of endometriosis.
Poster Session III

CELL CYCLE PROTEIN (P57) EXPRESSION AS A PROGNOSTIC MARKER IN OVARIAN CANCER

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Introduction: Epithelial Ovarian Cancer (EOC) accounts for more deaths than all gynaecological cancers combined. Despite extensive research, progress has been slow in understanding the pathobiology. EOC is identified as a heterogeneous malignancy with various histological subtypes showing differences in terms of presentation, response to treatment, immunohistochemical (IHC) reactivity and molecular profiling. Cell cycle deregulation is key in cancer development. p57kip2 is one such cell cycle regulator.

Methods: 250 tissue specimens from women with at least Stage 3 EOC were scored to assess IHC expression of p57kip2. These included chemo-naive tissue and those collected at interval debulking surgery following 3/4 cycles of chemotherapy. Complete clinical data from diagnosis was collected from notes and databases. Immunostain assessment was positive for a distinct brown staining in either nucleus or cytoplasm and scored independently by 2 assessors blinded to clinical outcome.

Results: Serous carcinoma was the commonest histological subtype in 88/250 (35.2%). IHC expression varied from strong to absent and appeared to be related to the morphological heterogeneity of EOC.

In univariate analysis, women with low p57kip2 expression were more likely to have advanced stage and grade of disease. This is associated with large volume of ascites, presence of macroscopic residual disease post surgery and shorter disease free interval and overall survival (p< 0.01).

Conclusion: High p57kip2 expression predicts good response to treatment and better prognosis suggesting the role of p57kip2 as a candidate biomarker of response to treatment and prognosis. Associated studies correlating IHC expression with mRNA and serum to confirm above are currently underway.
Poster Session III

RELEVANCE OF IMMUNOHISTOCHEMICAL EXPRESSION OF CYCLIN E IN EPITHELIAL OVARIAN CARCINOMA

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Introduction: Epithelial Ovarian Cancer (EOC) is the second common gynaecological cancer. Molecular mechanisms in EOC are poorly understood despite extensive studies. Cell cycle dysregulation is a hallmark of malignancy. Cyclins (CyclinE), mediates cell cycle progression and we hypothesized that overexpression may correlate with poor prognosis.

Materials and methods: 250 tissue specimens from women with at least Stage 3 EOC were scored to assess the IHC expression of CyclinE. The specimens included chemo-naive tissue as well as specimens collected at interval debulking following 3/4 cycles of chemotherapy. Complete clinical data from presentation was collected from notes and databases. IHC scoring was independently performed by 2 assessors blinded to clinical outcome. Normal ovaries, benign and borderline ovarian tumours were used as controls.

Results: CyclinE expression was noted across the spectrum of benign, borderline and invasive ovarian tumours with maximal expression in carcinomas. Overexpression was shown in high grade, advanced stage EOC and in serous and clear cell subtypes. Both univariate and multivariate analyses demonstrated overexpression in suboptimally debulked women and poor responders to chemotherapy. Significant association (p< 0.01) between overexpression and reduced disease-free interval and overall survival was noted.

Conclusion: CyclinE expression is progressively increased in tumour progression as well as in aggressive behaving carcinomas. Our results suggest that overexpression is an independent prognostic factor in EOC and maybe used to assess response to platinum based treatment and predict disease performance to treatment. Associated studies correlating IHC expression with mRNA and serum levels of CyclinE to confirm the above are currently underway.
Chemoresistance is one of the causes for poor survival in ovarian cancer. Mutations in Tp53 gene and/or activation of PI3K/Akt pathway are widely recognized factors for chemoresistance in several carcinomas including ovarian cancer. Interestingly, PIK3CA, phosphoinositide-3 kinase catalytic subunit alpha (α), is amplified rather than mutated in 16-24% ovarian carcinomas with association to platinum resistance and Tp53 mutations. In normal human ovarian surface epithelial cells (OSE), PI3KCA promoter is known to be negatively regulated by p53 protein. However, regulation of PIK3CA signalling during acquisition of chemoresistance in a wild-type p53 scenario has not been studied extensively. Herein, we aim to study the role of p53 in mediating PIK3CA signalling during development of resistance to cisplatin and paclitaxel in ovarian cancer cells. A unique PIK3CA sensor (PIK3CA promoter driving a bi-fusion reporter gene) was developed and introduced in A2780 cells, an undifferentiated ovarian cancer cells with wild type p53. We developed resistant models for cisplatin (70% viable) and paclitaxel (81% viable) using the above-mentioned cells by repeated exposure of increasing concentration of drugs. Both cisplatin and paclitaxel resistant models showed ablation of PIK3CA promoter attenuation with increased resistance. In cisplatin resistant model, this abolishment was corroborated with decrease in drug induced activation of Tp53. In both cisplatin and paclitaxel resistant cells, Akt, an immediate downstream target of PIK3CA, was activated by phosphorylation and localised to cell membrane. This study reveals that PIK3CA/AKT signalling is hyperactive and could be a potential target for the treatment in chemoresistant ovarian carcinoma.
Poster Session III

HIGH-GRADE SEROUS CARCINOMAS WITH OVARIAN AND ENDOMETRIAL INVOLVEMENT: ASSESSMENT OF CLINICAL CHARACTERISTICS, IMMUNOPHENOTYPE, AND SITE OF ORIGIN

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Introduction: High grade serous (HGS) cancers of the ovary (O) and endometrium (EM) share morphologic similarities and can be difficult to distinguish, particularly when both sites coexist. Treatment varies per site. An improved system of molecular phenotyping is needed.

Methods: Clinicopathologic and outcome data of optimally debulked HGSO&EM cancers were reviewed. Tissue microarrays taken from representative cores underwent immunohistochemistry (IHC) assessment of TP53, ER, PR, p16, and ARID1A. FT sectioning (SEE-FIMS) done on >600 gynecologic cases were reviewed to assess the rate of serous tubal intraepithelial carcinoma’s (STIC’s) in HGSEM cases. Exome capture was used for mutational profiling of STIC’s and concurrent EM lesions when found.

Results: 89 HGSO, 50 HGSEM and 43 HGS with both EM and O/FT involvement were analyzed (cohorts 1-3). The ovarian cohort was younger (mean 60 vs. 70/69yrs cohorts 2/3) and received more chemotherapy (97% vs. 51% vs. 25% cohorts 1-3, p< 0.0001). Progression free and overall survival were lowest in cohort 3 (p=0.0007) even with correction for stage. On IHC, HGSO had more aberrant TP53 expression (p=0.0031), and a higher proportion or ER+ cases (p=0.0004) than cohorts 2&3. Loss of ARID1A was a feature of 20% HGSEM and rare in HGSO (p=0.0008). Only TP53 expression distinguished outcomes between cohorts (p=0.0001). Three cases have been found with STICS and HGSEM cancer, sequencing results pending.

Conclusions: The clinical and molecular profile of HGS cancers with both EM and O/FT involvement appear most consistent with HGSEM cancers. Establishing the molecular pathways unique to these tumours will aid in classification and advance treatment strategies.
Poster Session III

CIRCADIAN PERIODICITY OF PLASMA LIPID PEROXIDES AND OTHER ANTIOXIDANTS AS PUTATIVE MARKERS IN GYNAECOLOGICAL MALIGNANCIES

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Introduction: The chronome (from chromos, time, and nomos, rule), or time structure, of lipid peroxidation and antioxidant defense mechanisms may relate to prevention and curative chronochemotherapeutic efficacy and management.

Aim: To investigate the circadian variation of lipid peroxide concentrations and antioxidant status of women with various gynecological malignancies as compared to clinical healthy women.

Material and methods: Newly diagnosed women with gynaecological malignancies (n=30), 30-60 years of age, and age matched clinically healthy women (n=35) provided blood samples every 6 hours for 24 hours under standardized conditions. Plasma Malondialdehyde (MDA), superoxide dismutase (SOD), Catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR) activities, and serum ascorbate, urate and high-density lipoprotein cholesterol (HDL-C) concentrations were determined.

Results: Each variable underwent circadian variation (p≤0.002). Patients differed from controls by their overall chronome-adjusted mean value (MESOR) and by the circadian dynamics in the spectral element of their chronome.

Conclusion: Chronomes of putative anti and pro-oxidants should be mapped to explore their putative chemotherapeutic role as markers in cancer chemoprevention and management of established disease.
Poster Session III

LIPOCALIN2 ENHANCES THE PROLIFERATION OF ENDOMETRIAL CARCINOMA CELLS IN NUDE MICE

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Background: We previously reported that lipocalin2 (LCN2), a molecule involved in iron-transport, was up-regulated in endometrial carcinoma, and the over-expression of LCN2 with its receptor, SLC22A17, was associated with poor outcome of the patients with endometrial carcinoma. To further examine the molecular function of LCN2, we examined the cell viability under ultraviolet (UV) irradiation or cisplatin (CDDP) treatment in vitro, and the tumor growth in nude mice.

Methods: LCN2-silenced HHUA (originally over-expressing both LCN2 and SLC22A17) were established using shRNA producing vector. The viability of these HHUA cells after UV irradiation or CDDP treatment was measured by WST-1 assay. Those HHUA cells were then injected to nude mice subcutaneously. The size of subcutaneous tumors was measured.

Results: After UV irradiation, the mean reduction ratio of the viable LCN2 silenced HHUA cells (74.6% reduction) was significantly larger than that of control HHUA cells (48.8%, p< 0.05). After CDDP treatment to HHUA, LCN2-silencing significantly reduced the residual viability (77.6% to 37.1%) (p< 0.05). However, these differences were dissolved by iron-chelation. The growth of LCN2-silenced HHUA showed no difference with that of control HHUA in vitro. However, LCN2-silencing significantly reduced the tumor growth in nude mice (84% reduction). Moreover, the down-regulation of phospho-Akt expression was observed in tumors of LCN2-silenced HHUA.

Conclusions: LCN2 is involved in the survival of endometrial carcinoma cells and the tumor growth in vivo, via p-Akt signaling and the control of intracellular iron concentrations.
Poster Session III

CANCER-DERIVED TISSUE FACTOR AND COAGULATION FACTOR VII ARE CONTRIBUTING TO THE VENOUS THROMBOEMBOLISM IN UTERINE CERVICAL AND ENDOMETRIAL CARCINOMAS

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Background: In cancer patients, the risk for venous thromboembolism (VTE) is high. Although tissue factor (TF) is spotlighted as a cancer-cell derived coagulant, participation in VTE has not been clarified. We raised a possibility that cancer-cell-derived coagulation factor VII (fVII) develops into active TF/fVIIa complex on cancer cell surface, which is a highly potent initiator of coagulation, and that the complex is secreted as microparticles into the environment. The object of this study is to investigate the expression of TF and fVII, and further the functional TF/fVIIa formation in uterine cancer cells, and also their implication in VTE.

Methods: The TF/fVII expression was evaluated in seven cervical and five endometrial carcinoma cell lines by qRT-PCR, Western blotting and fXa generation. For clinical cases, immunohistochemistry for TF was performed.

Results: The TF/fVII expression was proven in all cell lines examined, especially high in cervical carcinoma SKG-I, II, IIIa and CaSki. However, the TF/fVIIa activity was not simply associated with the expression levels of TF or fVII in cells. Although TF expression was revealed in more than 80% of clinical tumors, no positive association with VTE was found. Further analysis showed that tissue factor pathway inhibitor-1 (TFPI-1) was also expressed in cell lines in different levels.

Conclusions: We first elucidated a wide expression of TF on a series of cell lines and clinical tissues in cervical and endometrial carcinomas. However, no significant relation between TF expression level and VTE was revealed. Expression of TFPI-1 might be involved this observation.
Poster Session III

APPLICATION OF FOURIER-TRANSFORM INFRARED SPECTROSCOPY TO DISCRIMINATE LOW-RISK AND HIGH-RISK HPV SUBTYPES

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Background: Application of infrared (IR) spectroscopy appears to be a novel approach which can characterise biomolecular alterations in cervical cytology.

Aim: To determine whether IR spectroscopy combined with multivariate analysis could be applied to discriminate exfoliative cervical cytology according to HPV status.

Methods: Cervical smear specimens (n=350) were collected and classified as low-grade (mild dyskaryosis), high-grade cytology (moderate & severe dyskaryosis) and cancer. The samples were then sub-typed into high and low-risk HPV categories.

Aliquots of 1-2 ml of specimen were centrifuged and the supernatant aspirated. The remaining cell pellet was resuspended in d.H2O and centrifuged before being transferred to low-E glass microscope slide. Spectroscopic interrogation was performed using a Bruker Vector 22 FTIR spectrometer. IR spectra were acquired from 10 locations per slide using a CCTV camera. Linear Discriminate Analysis was applied to generate score plots in order to identify category segregation and cluster vector plots towards biomarker extraction.

Results: Excellent discrimination was obtained between low-grade, high-grade and normal cytology. Visual inspection of the derived IR spectra suggests that the 1155cm⁻¹ - 960cm⁻¹ region best discriminates different categories. The peaks which mainly discriminate HPV subtypes are 1211cm⁻¹ and 1400cm⁻¹, which correlate with backbone structural alterations in DNA and RNA, phosphates and phospholipids. Spectral differences between low-risk and high-risk HPV-infected cytology were statistically significant (P < 0.05).

Conclusion: HPV status is discernible employing IR spectroscopy. Our results point to a novel biomarker extraction approach that could be applied to better triage patients independent of conventional measures of HPV status.
LYMPHOMA OF THE FEMALE GENITAL TRACT

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Malignant lymphomas in the female genital tract are rare, and those arising from this tissue system are extremely uncommon. Twenty five percent of malignant lymphomas arise at extra nodal sites and in only one percent of women with extra nodal tumours is the genital tract involved. Clinical symptoms are often non-specific and mimic other more common gynaecological malignancies.

We present a series of 15 patients who presented to the Mercy Hospital for Women in Melbourne, Australia with pelvic pathology. This was a retrospective study of patients who presented from 1988 to 2010. Mean age at presentation was 62 years. The adnexae were involved in 5 cases, followed by the vulva in 2 cases and 1 case involving the vagina. There were 3 cases of endometrial endometrioid adenocarcinoma with lymph nodes positive for lymphoma. Interestingly 2 cases presented as pelvic masses, one in the Pouch of Douglas and the other a soft tissue mass close to the external iliac vessels. Biopsies of these confirmed lymphomas. As expected, the majority of cases were non-Hodgkin’s Lymphoma of B cell phenotype.

In most cases of lymphoma of the female genital tract it is difficult to determine primary versus secondary disease especially when the disease is advanced. It is a diagnostic challenge when not suspected.
Poster Session III

ANTI-CANCER PEPTIDE PNC-27 IN VIVO: POTENT CYTOTOXICITY AGAINST AND GROWTH INHIBITION OF OVARIAN CANCER IN A RODENT MODEL

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PNC-27 is a novel anti-cancer peptide synthesized of AAs 12-26 of the p53-HDM2 binding domain and a novel membrane delivery sequence (MRP, 16 AAs). In vitro and in vivo PNC-27 is selectively cytotoxic against cancer (CA) cells while leaving normal including hematopoietic stem cells unaffected. Studies indicate that PNC-27 forms transmembrane pores in CA cells causing rapid necrotic cell death. Since ovarian cancer is the leading cause of death from gynecologic malignancies, we examined the effect of PNC-27 on primary ovarian neoplasia in a syngeneic and immuno-competent disease model. After establishing effective cytotoxicity of PNC-27 against ID8 ovarian CA cells (LD50 =120 ng), syngeneic C57/BL6 mice were inoculated subcutaneously with ID8 cells. When tumors reached >150 mm³, 24 mice were randomized to groups (A, n=11) for daily intra-peritoneal injections (i.p.I.) of PNC-27; (B, n=4) for weekly i.p.I. of carboplatin - paclitaxel (C/T), and (C, n=9) no treatment (i.p.I. PBS). Tumor sizes were recorded daily for 28 days. Statistical analysis by a linear mixed model shows that tumor growth was significantly different between treatment groups (F(2,493)=10.6, p< 0.001): The mean tumor size difference between groups (A) & (C) was 468.5 units (t(493)=4.25, p<0.001); the difference between (B) & (C) was 468.3 units (t(493)=2.84, p=0.005). No significance was found between (A) & (B) (p=0.99). In the absence of toxic effects on hematopoiesis and cytotoxicity against the ovarian CA cells equivalent to the standard C/T therapy, the results strongly suggest that PNC-27 is ideally suited for effective long-term ovarian cancer therapy.
Poster Session III

HUMAN PAPILLOMAVIRUS PERSISTENCE IN YOUNG UNSCREENED WOMEN, A PROSPECTIVE COHORT STUDY

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Objective: To evaluate hr-HPV persistence and associated risk factors in a prospective cohort of young unscreened women, as well as cytology/histology follow-up.

Methods: Two year follow-up of 235 out of 2065 women (18-29 years), participating in a prospective epidemiological study, with questionnaires, self-collected cervico-vaginal samples, and SPF(10)LiPA HPV detection. Only women hr-HPV positive at sample month 12 were invited for a second year of follow-up. After study follow-up, available cytology/histology data were compared with the month 12 hr-HPV negative women from the same cohort.

Results: 44.1% of the hr-HPV types detected at study month 12, persisted during follow-up. HPV types 45, 31, 16 and 18 were most likely to persist with 60.0%, 56.8%, 54.4%, and 50.0% persistence, respectively. Infections present since 6 months or baseline had an increased risk to persist (OR 3.09 [95% CI: 1.74-5.51] and OR 4.99 [95% CI: 2.67-9.32], respectively) compared with newly detected infections. Other co-factors influencing persistence were, multiple HPV infections, smoking and multiple lifetime sexual partners. HSIL/CIN2+ was detected in 12.1% of the persistent HPV group, in 5.3% of the women who cleared the hr-HPV infection, and in 1.6% (P< 0.001) of women in the hr-HPV negative control group.

Conclusion: We showed that HPV genotype, multiple infections, smoking, and multiple lifetime sexual partners are co-factors that increase the risk of hr-HPV persistency. Most importantly, we showed that hr-HPV infections are more likely to persist the longer they have been present and that women with a persistent hr-HPV infection have a high risk of HSIL/CIN2+ development.
Poster Session III

CANCER SCREENING BEHAVIORS AND FACTORS AFFECTING CANCER SCREENING BEHAVIORS IN TURKISH WOMEN

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Aim: National cancer screening program includes mammography to screen for breast cancer, colonoscopy and fecal occult blood stool test for colorectal cancer, and Pap smear test for cervical cancer in Turkey. The aim of this study was to explore the cancer screening behaviors and factors affecting cancer screening behaviors in Turkish women.

Methods: A survey with self reported questionnaire was conducted on 603 Turkish women between 30-70 ages.

Results: The mean age of women was 44.50±6.67 years and all of them were married. More than half of the women (56.4%) had heard national cancer screening program. It was found that 48.2% of women over 50 years had received mammography screening at least one time during their life time. For women over 50 years, the rate of having colonoscopy and fecal occult blood stool test were 12% at least one time during their life time. It was found that 32.8% of women over 30 years had a Pap smear test at least one time during their life time. It was also found that some factors such as knowing national cancer screening program, knowing why mammogram/pap smear test is done affected women’s breast/cervical cancer screening behaviors.

Conclusion: The rate of women having mammography, pap smear test, colonoscopy, and fecal occult blood stool test was moderately low in Turkish women. It is suggested that organizing educational programs directed at increasing women’s level of knowledge about national cancer screening and methods of early diagnosis would be beneficial.
Poster Session III

MICRORNA 146A IS A POTENTIAL URINARY BIOMARKER OF OVARIAN CANCER

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Objectives: MicroRNAs (miRNAs) are small noncoding RNA regulators of gene expression implicated in cancer pathogenesis. The aim of this study was to delineate miRNAs present in urine of ovarian cancer subjects, and to identify therapeutic gene targets of urinary miRNAs.

Methods: Urine samples were obtained at ovarian cancer cytoreduction from subjects giving informed consent under an IRB approved protocol. Trizol was added to 100ul of urine and frozen at -70°C. miRNA was isolated using a Qiagen miRNA Easy kit. Multiple urine samples from each subject were combined to obtain miRNA profiles of 5 by deep sequencing analysis. Expression of urine miRNAs were confirmed by qRT-PCR from additional subjects. Established ovarian cancer cell lines with known BRCA1 status (PEO4, PEO6, SNU251) were cultured under standard conditions in RPMI with 10% serum. miRNA reagents were obtained from Qiagen.

Results: miRNA 146a was defined as a potential differentially expressed urinary miRNA. miR146a targets BRCA1 and NM23. Confirmation of miRNA146a specificity for BRCA1 and NM23 was performed through transient overexpression of miRNA146a, with target downregulation detected by western blot. Overexpression of miR146a was confirmed by qRT-PCR. Expression of miRNA146a was detected in the urine of 10 ovarian cancer subjects, but was absent from normal subjects.

Conclusions: miRNA 146a is predicted to target tumor suppressor genes important in ovarian cancer, BRCA1 and NM23. Increased expression of miRNA 146a would be expected to block the expression of these two tumor suppressors and its presence in urine of ovarian cancer subjects may provide a potential urinary biomarker.
Poster Session III

KNOCKDOWN OF HEAT SHOCK PROTEIN 70 EXPRESSION SUPPRESSES CELL MIGRATION, INVASION AND PROLIFERATION ACTIVITIES IN UTERINE CERVICAL CANCER CELLS

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Objective: Heat Shock Protein 70 (HSP70) was identified as high level expressed protein in uterine cervical squamous cell carcinoma (SCC). We investigated the role of HSP70 in cancer cell behaviors of uterine cervical SCC cell lines in vitro.

Methods: To investigate the role of HSP70, small interfering RNA (siRNA) was used to knockdown HSP70 expression. The effects of HSP70 expression on cancer cell migration, cell invasion, cell proliferation activities, cell cycle status and apoptosis were examined. Furthermore, the effects of HSP70 expression on apoptosis induced by cisplatin (CDDP) treatment were examined.

Results: Knockdown of HSP70 expression significantly suppressed cell migration and cell invasion activities. The cell proliferation activities were also suppressed by arresting at S and G2/M-phase in cell cycle and inducing apoptosis. Furthermore, the percentage of apoptosis induced by CDDP treatment was significantly built up by knockdown of HSP70 expression.

Conclusions: Our data clearly suggested that knockdown of HSP70 expression suppressed cell migration, cell invasion and cell proliferation activities, and built up the effect of apoptosis induced by CDDP treatment. HSP70 may become an useful molecular target therapy for treatment of uterine cervical SCC.
Poster Session III

ANALYSIS ON THE POTENTIAL TRANSCRIPTIONAL FACTORS ASSOCIATED WITH CISPLATIN RESISTANT IN OVARIAN CANCER CELLS

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Objective: To analysis the potential transcriptional factors associated with cisplatin chemotherapy resistant.

Methods: We used ovarian cancer cell line SKOV3 and its cisplatin resistant cells SKOV3-DDP as a pair of drug sensitive and drug resistant in vivo cellular model. The cellular apoptosis of SKOV3 and SKOV3-DDP was compared by flowcytometer after treatment with 2mg/ml, 5mg/ml and 8mg/ml concentration of cisplatin. Furthermore, 345-channel Protein/DNA array was used to analysis the potential transcriptional factors with cisplatin related resistant in these cell lines.

Results: In total 345 candidate transcriptional factors, 53 transcriptional factors were associated with ER status. Compared with SKOV3 cell, the 31 transcriptional factors activities were up-regulation and 22 were down-regulation SKOV3-DDP cell.

Conclusion: Transcriptional factors microarray is a useful tool to screen the potential transcription factors associated with cisplatin resistant in ovarian cancer.
Poster Session III

THE TRANSCRIPTIONAL FACTORS AFFECTED BY ESTROGEN RECEPTOR-RELATED RECEPTOR-A IN ENDOMETRIAL CANCER CELL HEC-1A ANALYSIS BY OLIGONUCLEOTIDE ARRAY-BASED TRANSCRIPTION FACTOR ASSAY

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Objective: To analysis the transcriptional factors activity in endometrial cancer cell Hec-1A with different expression of estrogen receptor-related receptor alpha.

Method: A recombinant plasmid with green flor protein label and G418. A stable cell lines with over-expression of ERRalpha was constructed. The mRNA expression of ERR was detected by quantitative RT-PCR and protein expression was detected by Western-blot. Furthermore, 326 chanel Oligonucleotide Array-based Transcription Factor Assay (OATFA) was used to analysis the transcriptional factors activity in HEC-1A, HEC-1A/empty, HEC-1A/ERR.

Results: In total 326 candidate transcriptional factors, 7 transcriptional factors showed different activities with different expression of ERR level. Compared with HEC-1A/empty, 3 transcriptional factors activities are up-regulation and 4 are down-regulation in ERR high expression HEC-1A/ERR cell. Over-expression of ERR down-regulated the transcriptional activities of SREBP, AP-1, c-Myc, Usf-1/2, while up-regulated transcriptional activities of RFX-1, PPAR-α, PPAR-γ.

Conclusion: Transcriptional factors SREBP, AP-1, c-Myc, Usf-1/2 RFX-1, PPAR-α, PPAR-γ are ERRα targeted transcriptional genes, while OATFA is an useful tool to screen the genes match the transcriptional factor.
Poster Session III

ANALYSIS OF CELL IMMUNE FUNCTION IN PATIENTS WITH GYNECOLOGY MALIGNANT TUMOR

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Objective: To investigate the immune function and its clinical significance in patients with gynecology malignant tumor.

Methods: Peripheral blood lymphocyte subsets were detected by flow cytometry in 108 cases with gynecological malignant tumor and 17 healthy cases. Results In the patients with cancers, the proportion of CD4⁺ T lymphocyte, natural killer cell, and the CD4⁺/CD8⁺ ratio were increased, while CD3⁺, CD8⁺ T lymphocyte were decreased significantly, compared with normal control (P< 0.05). The proportion of CD19⁺ (B lymphocyte) showed no difference between the two groups (P>0.05).

Conclusion: In patients with gynecological malignant tumor exists immune dysfunction. The detection of peripheral blood T lymphocyte subsets and NK cell can be used as one of the indicators of cell immune dysfunction.
Poster Session III

PROGNOSTIC SIGNIFICANCE OF TUMOR INFILTRATING LYMPHOCYTES (TILS) IN GYNECOLOGICAL CANCERS

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Objective: Tumor infiltrating lymphocytes (TILs) are considered to be a manifestation of the host immune response against cancer cells. CD8+, CD4+ T, FOXP3+ T cells and NK/NKT cells that represent adaptive and innate immunity respectively are the most likely effector TILs. The aim of this study was to summarize the prognostic significance of particular subtypes of TILs in gynecological cancers by analyzing PubMed database.

Methods: Published studies that evaluated the association between TILs and patient survival in vulvar, cervical, endometrial and ovarian cancer were identified. Data were extracted from papers that met criteria and further evaluated.

Results: Suitable studies comprising 1815, 623, 387, 358 patients with ovarian, endometrial, cervical and vulvar cancer respectively were analyzed. CD8+ T cell infiltration and CD8+/FOXP3+ index were predictors of better outcome in ovarian cancer. CD8+/FOXP3+ index was found to be independent prognostic factor in endometrial cancer. CD8+ infiltrates and CD8+/CD4+ index were correlated with longer OS in HPV-positive cervical cancer inversely to intratumoral FOXP3+ T cells. Lack of prognostic significance of TILs was found in vulvar cancer. Prognostic significance of NK/NKT was not assessed in gynecological cancers. Variations in the prognostic value of TILs based on debulking status, scoring method and geographic regions were identified.

Conclusion: TILs are predictors of outcome in ovarian, endometrial and cervical cancer and could define a specific class of patients whose tumor biology should be taken into account in therapeutic strategies. Methods of evaluation and quantification of immune cells within epithelial malignancies need to be unified for future studies.
Poster Session III

TRIPTOLIDE HAS A PROFOUND ANTI-GROWTH ACTIVITY IN ENDOMETRIAL AND OVARIAN CANCER CELLS

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Background: Triptolide (TPL), a bioactive component of the Chinese medicinal herb Tripterygium wilfordii Hook F, induces apoptosis in some lines of human tumor cells. We investigated the effects of TPL on three endometrial and two ovarian cancer cell lines.

Methods: Endometrial and ovarian cancer cells were treated with various concentrations of TPL, and its effects on cell growth, cell cycle, and apoptosis were investigated. Furthermore, we examined global changes in gene expression in HHUA endometrial cancer cells after treatment with TPL. By using a list of 20 differentially expressed genes, Western blot analyses were performed on five endometrial and ovarian cancer cell lines.

Results: All endometrial and ovarian cancer cell lines were sensitive to the growth-inhibitory effect of TPL. Cell cycle analysis indicated that their exposure to TPL increased the proportion of cells in the S-phase of the cell cycle. Induction of apoptosis was confirmed by annexin V assay and loss of the transmembrane potential of mitochondria. cDNA microarray assay demonstrated that the treatment with TPL induced the up-regulation of cell cycle regulators and apoptosis-inducing factors and the down-regulation of cell proliferation markers. Of these genes inducing TPL treatment, up-regulation of LRAP, CDH4, and SFRP1 and down-regulation of cystatin, TNNT1, and L1-CAM were confirmed using Western blot analysis in all the cell lines examined.

Conclusions: We found a strong anticancer activity of TPL and identified the potential target genes of this drug, raising hopes that TPL may become a useful therapy for endometrial and ovarian cancers.
Poster Session III

EXPRESSION AND CYTOPLASMIC LOCALIZATION OF SAM68 IS INDEPENDENT PROGNOSTIC FACTOR FOR PATIENTS WITH EPITHELIAL OVARIAN CANCER

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Objective: The role of Sam68 in carcinogenesis remains controversial. This study was aimed at investigating the expression profile of Sam68 and its clinical/prognostic significance in epithelial ovarian cancer.

Methods: Quantitative polymerase chain reaction (qPCR) and western blotting were performed in ovarian cancer cell lines and fresh epithelial ovarian cancer and paired adjacent non-cancerous ovarian tissues. Then, immunohistochemical staining for Sam68 was performed in 279 paraffin-embedded tissue sections.

Results: Sam68 expression in ovarian cancer cell lines and cancerous tissues was significantly up-regulated at both protein and mRNA levels compared to that in normal ovarian tissues. The high expression level of Sam68 and its cytoplasmic localization were significantly associated with tumor grade (P = 0.014), cytoreductive status (P = 0.035), and most importantly FIGO stage (P < 0.001). Multivariate analysis showed that high expression level of Sam68 protein and its cytoplasmic localization served as significant and independent prognostic factors of poor overall survival and disease-free survival in patients with epithelial ovarian cancer.

Conclusion: Sam68 expression and cytoplasmic localization were inversely correlated with survival of epithelial ovarian cancer patients, and could represent a novel prognostic marker for ovarian cancer.
Poster Session III

DISULFIRAM (ANTABUSE) ACTIVATES THE UNFOLDED PROTEIN RESPONSE TO OVERCOME CHEMORESISTANCE IN OVARIAN CANCER CELLS

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Objectives: The unfolded protein response (UPR) is a mechanism whereby cells respond to environmental and chemical challenges affecting the secretory pathway. Small molecules that induce prolonged UPR lead to apoptosis. We hypothesized that sustained UPR activation in ovarian cancer would lead to cell death regardless of platinum chemosensitivity.

Methods: Seven established ovarian cancer (OVCA) cell lines (3 platinum sensitive and 4 platinum resistant) and two primary OVCA cell lines were studied. Cells were cultured with disulfiram ± reactive oxygen species (ROS) scavengers. Cells were analyzed for proliferation, cellular death and the accumulation of UPR- and apoptosis-related mRNA transcripts. Athymic mice with tumor-xenografts containing a stable Chop-luciferase reporter were gavaged with disulfiram and evaluated with bioluminescent imaging.

Results: Disulfiram (IC50 4-12 µM) potently reduced proliferation by 24 hours with up-regulation of UPR- and apoptosis-related gene transcripts noted by six hours. FACS analysis revealed an increase of annexin-positive cells along with loss of mitochondrial membrane potential signified by increased JC-1. Cell death was significantly inhibited by the addition of ROS scavengers. Murine fibroblasts null for Chop were resistant to disulfiram and demonstrated delayed caspase activation, suggesting the UPR was a critical regulator of disulfiram-induced cell death. Importantly, orally administered disulfiram activated a Chop-luciferase reporter in a tumor xenograft model.

Conclusion: OVCA cells, regardless of platinum sensitivity, were susceptible to prolonged UPR activation by disulfiram. Disulfiram, a well tolerated, orally bio-available agent should be studied further as a novel therapeutic for the treatment of chemoresistant ovarian cancer.
Poster Session III

FIBRINOGEN AND PLATELET GLYCOPROTEIN IB ALPHA IS NOT CRUCIAL FOR THROMBIN-DEPENDENT BREAST CANCER METASTASIS IN HYPERTHROMBOTIC TM^PRO^ MICE.

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Background: The coagulation activation initiated by tissue factor (TF) on tumor cell supports fibrin formation, platelets activation that contributes to the survival of arrested metastases in the vasculature of the lung. Here we address the contribution platelet, platelet glycoprotein (GP) Ibα and fibrinogen to the markedly enhanced metastasis in hyperthrombotic thrombomodulin mutant (TM^PRO^) mice.

Methods: Mouse mammary carcinoma cells (line 3503) and the TF knockout cells established from 3503 were injected in wild type and TM^PRO^ mice intravenously, and then the lungs were harvested and counted the numbers of metastases. Mice were given intraperitoneal injection of anti glycoprotein 1bα antibody (5A7) to deplete platelets and reconstituted intravenously with the platelets expressed human GPIbα (hGPIbα^+^) and IL-4R chimera as control. 25KU/kg of Batroxobin was injected intravenously to deplete fibrinogen.

Results: TM^PRO^ mice showed high metastatic phenotype. Lung metastasis was dependent on TF on tumor cell and platelet. The reconstitution with either platelet genotype restored metastasis in wild-type or TM^PRO^ mice. The number of metastases in WT mice reconstituted with IL-4R expressing platelets was slightly lower compared to mice reconstituted with hGPIbα^+^ platelets. However, no appreciable differences were observed in reconstituted TM^PRO^ mice. Fibrinogen depletion markedly diminished the pulmonary metastases in wild type mice but not in TM^PRO^ mice.

Conclusion: Pulmonary metastasis in TM^PRO^ mice is highly dependent on platelet and independent on platelet GPIbα and fibrinogen.
Poster Session III

IN VIVO ANTI-TUMOR EFFECTS OF CORD-BLOOD DERIVED DCS INDUCED BY SCD40L ON OVARIAN CANCER CELLS

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Objective: To study the anti-tumor effects of dendritic cells (DCs) from cord blood stimulated by sCD40L in vitro.

Methods: The expressions of CD80 and CD86 on DCs stimulated by sCD40L were identified by FCM and CMLS. The secretions of IL-23, IL-27, STAT4, T-bet, CCR7, IL-10 and TGF-β mRNA from DCs stimulated by sCD40L were detected by RT-PCR. Moreover, the level of TNF-α and IL-23 in DCs supernatants were determined by ELISA. The ability of DC induced by sCD40L to stimulate the proliferation of T lymphocytes was determined by MLR. IFN-γ mRNA in co-cultured T cells and DCs was detected by RT-PCR. The specific cytotoxicity of CTL induced by sCD40L and DCs loaded melted antigen was detected by MTT.

Results: The expressions of CD80 and CD86 on DCs cultured with sCD40L were obviously increased. The expression of IL-23, IL-27, STAT4, T-bet, CCR7 mRNA on DCs stimulated by sCD40L were much higher, so were IL-23 and TNF-α protein. However, the expressions of IL-10 and TGF-β mRNA were much lower. The level of IFN-γ secreted by T cells cocultured with DCs in GM-CSF+IL-4+SCF+Flt-3l+sCD40L group was significantly higher. The specific cytotoxicity of CTL induced by sCD40L and DCs loaded melted antigen was much stronger.

Conclusions: The joint effect of sCD40L with a variety of cytokines could activate cord blood DC and induce its maturation and facilitated T lymphocytes differentiated into Th1 through the upregulation of STAT4/T-bet, which provides new ideas about the application of sCD40L in the tumor clinical immunotherapy.
Poster Session III

ROLE OF IL-12P40 IN CERVICAL CARCINOMA

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The local cytokine and chemokine microenvironment is important for tumor progression. Previously, we have shown that low IL-12p40 mRNA expression by cervical cancer cells is associated with poor survival of cervical cancer patients. Since IL-12p40 is both a subcomponent of IL-12 (composed of IL-12p40 and IL-12p35) and IL-23 (composed of IL-12p40 and IL-23p19) the aim of this study was to elucidate the role of IL-12p40 in cervical cancer. For this purpose we have measured the expression of IL-23p19 mRNA using mRNA in situ hybridization and compared its expression with IL-12p35 and IL-12p40 expression. Since IL-23 is a component of the IL-17/IL-23 pathway, a pathway induced by IL-6 in humans, we have also studied IL-6 expression, using immunohistochemistry. In contrast to IL-23p19 expression, IL-23 expression was significantly associated with poor disease-specific survival (P=0.017). Also a high number of stromal IL-6 positive cells was shown to associate with poor disease-specific survival (P< 0.001). The worst disease-specific survival was associated with a subgroup of patients that displayed a high number of IL-6 positive cells and IL-23 expression (P< 0.001). Furthermore, both a high number of IL-6 positive cells and a high number of IL-6 positive cells plus IL-23 expression were shown to be independent clinico-pathological parameter compared to lymph node metastasis, parametrial involvement and Sedlis score (P=0.009 and P=0.022, respectively). Our results support the hypothesis that IL-23 plays a suppressive role in cervical cancer.
Poster Session III

ACUTE SIDE EFFECTS OF INTRAOPERATIVE ELECTRON RADIOTHERAPY OF BREAST CANCER

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Purpose: Intraoperative boost irradiation as part of breast-conserving therapy is a perfect method to adequately capture the high risk tumor relapse area. Intraoperative radiotherapy (IOERT) as a boost for breast cancer releases a high single dose of radiation to the breast tissue; therefore acute toxicity is of particular attention. We therefore analyzed the acute toxicity after radiotherapy with 10 Gy as a boost with a minimum follow-up of 3 months.

Materials and methods: A total of 69 patients treated with IOERT (10Gy with 5, 7 and 9 MeV electrons) with a dedicated robotic linac (NOVAC 7, New Radiant Technology, Aprilia, Italy) to the tumor bed during breast-conserving surgery as a boost followed by whole-breast radiotherapy (WBRT, 50.4 Gy; 1.8 Gy per fraction) were included in this study. All patients underwent a retrospective follow-up (median, 8 months; range 1-17 months) regarding acute side effects within the first three months. Toxicities were documented using the common toxicity criteria (CTC 4.0 of the European Organization for Research and Treatment of Cancer).

Results: The IOERT was well tolerated. As a side effect there was one patient with seroma. Two patients developed chronic pain in the irradiated breast. Two patients developed a secondary wound healing. The remaining patients did not develop any grade 3 or 4 side effects. The observed toxicity rates were not influenced by age, tubus size, electron energy or systemic therapy.

Conclusions: After IOERT of the breast using electrons we did not find any unexpected acute toxicity rates.
HEMANGIOSARCOMA AFTER BREAST CONSERVING THERAPY OF BREAST CANCER, REPORT OF SEVEN CASES
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Background: Hemangiosarcomas of the breast represent a rare disease of the breast mainly occurring as secondary neoplasias with a latency of 5-10 years after primary treatment of breast cancer and are associated with an unfavourable prognosis. Radiation therapy, which is integrated within the concept of breast conserving therapy ranks as the main risk factor.

Patient and method: In this report we describe the clinical course of 7 patients including their molecular genetic pattern and give a summary of the actual literature.

Results: Haemangiosarcomas occur as a secondary neoplasm with a latency of 5-10 years after primary treatment of breast cancer and have an unfavorable prognosis. A genetic predisposition is assumed, but we could not find a significant role of tumor suppressor genes BRCA1, BRCA2 or p53 in our patients.

Conclusion: Due to limited available data for these tumours, recommendations for therapy include radical tumour resection achieving wide free margins and inconsistent regimens of chemo- and/or immune-therapy modalities. In the majority these are orientated on the systemic therapy-regimens for other cutaneous sarcomas, such as Kaposi's sarcoma. Efforts should be taken for a nationwide systematic registration of all cases of post-irradiation hemangiosarcomas.
Poster Session III

COMPARISON OF MENOPAUSAL SYMPTOMS IN WOMEN WITH AND WITHOUT BREAST CANCER

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Background and objective: Breast cancer is the most common cancer among women, comprising about 23% of all cancer types. According to some studies in women with menopausal symptoms may be different than the healthy women. The aim of present study was to determine the menopause symptoms in women with breast cancer compare with women without breast cancer.

Methods and materials: In this study, postmenopausal women aged 40-65 years old who referred to medical centers affiliated to Babol University of Medical Sciences, due to menopausal symptoms, was enrolled. A group of 80 women with breast cancer considered as group case (group A) and 100 women without breast cancer considered as group control (group B). After obtaining informed consent, a checklist including symptoms of menopause were completed in both groups, to compare the two groups. Data entry into statistical software SPSS 18 using T-Test and chi-square tests were analyzed. P < 0.05 was considered significant.

Result: During past 4 weeks, depression in group A and insomnia in group B was significantly higher (p=0.026 and p=0.027, respectively). But other menopausal symptoms were not significantly different in two groups.

Conclusion: According to the results of this study, Menopausal symptoms in breast cancer patients have not so much different to patients without breast cancer.
Poster Session III

PROGNOSIS AND SURVIVAL OF MEN WITH METASTATIC BREAST CANCER

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Introduction: About 1% of breast cancers occur in men, respectively ~500 new cases per year in Germany. Clinical studies on breast cancer in men are limited for case studies or retrospective analysis. In the recent years no studies have been published on the clinical course of metastatic breast cancer in men. Therefore we here present a retrospective cohort study on this topic.

Patients and methods: Clinical and pathological tumor characteristics and follow up of male breast cancer patients with metastatic disease diagnosed in the region Chemnitz / Zwickau in the state of Saxony 1995-2011 were documented and statistically evaluated.

Results: 41 men with metastatic breast cancer; 15 (36.6%) with primary metastasis. Median survival time: 38 months. Most common localizations of metastasis: bones (n=23), lungs (n=21), liver (n=8). If a systemic therapy was given the prognosis was significantly improved (p< .004). The systemic therapy in the metastatic state was very heterogeneous and consisted of endocrine therapy and / or chemo therapy. In 15 (36.6%) cases palliative radio therapy was administered. The initial tumor characteristics (size, nodal state, grading) were not of any prognostic relevance on future development of metastasis. Prognostic unfortunate were a negative hormone receptor state (p< .001) and triple negative receptor state (n.s.).

Discussion: Metastatic male breast cancer patients had a comparatively good prognosis and showed significant benefit from systemic therapy. In patients with negative receptor state and without systemic therapy the prognosis was especially worsened. Up-to-date systemic therapy may improve survival in men with metastatic breast cancer.
Poster Session III

SINGLE INSTITUTION STUDY OF YOUNG BREAST CANCER (≤ 35 YEARS) FROM NORTHERN INDIA

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Background: Breast cancer in young women (≤ 35 years) is uncommon and accounts for 1-2 % of all breast cancer in the West. There is paucity of data on young breast cancer from India. The aim of our study was to assess clinical and pathological parameters and outcome in young breast cancer patients.

Methods: This analysis was carried out in 194 patients with aged 35 years or less, who were registered in our clinic between 2000-2009.

Results: The median age was 31 years (range 21-35). The median duration of symptoms was 11.8 months (range 0.5-40). Breast lump was the commonest (93%) presenting symptom (left >right side). Stage distribution was stage I was 3 %, stage II- 20%, stage III- 55%, and stage IV- 22%. The median clinical tumour size was 5.9 cm. Modified Radical mastectomy was the commonest surgical procedure. 94% was IDC, 60% of tumours were high grade and 56% had pathological node positive disease. ER/PR and her2neu positivity was 40% and 30% respectively. Triple negative breast cancer (TNBC) constituted 31%. With a median follow up of 30 months, three years progression free (PFS) was 24 months and overall survival (OS) 60%. Higher Nodal stage, tumour size (>5 c.m), negative ER/PR status and visceral metastasis at baseline predicted poor outcome.

Conclusion: Young women constituted 5.5 % cases with higher proportion of triple negativity, this is higher than the western population reflecting younger age of our population of breast cancer in general with a resultant poorer outcome.
A REVIEW OF BREAST CANCER CASES THAT WERE DIAGNOSED DURING PREOPERATIVE EVALUATION IN A GYNECOLOGIC ONCOLOGY UNIT

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Aims: To review results of breast cancer cases which were diagnosed incidentally during preoperative evaluation in gynecologic oncology outpatient unit. All of the operations were performed in Zekai Tahir Burak Women’s Health and Research Hospital, which is a tertiary referral center for women’s diseases located in Ankara, Turkey.

Methods: Hospital cancer registry database was reviewed for breast cancer cases recorded between January 2007 and December 2011. Patients who were evaluated and treated in gynecological oncology unit were included in the study.

Results: A total of 49 cases were identified and included in the study. Mean patient age was 52.5±9 years. Twenty cases (40.8%) were asymptomatic, 13 (26.5%) had abnormal nipple discharge, 12 (24.5%) had a self-palpated mass, and 4 (8%) had breast pain. Twelve cases (24.5%) were being evaluated for an adnexal mass, 19 (38.8%) for cervical dysplasia, 14 (28.6%) for endometrial hyperplasia, and 4 (8.2%) for postmenopausal bleeding. Twelve cases (24.5%) had normal previous mammographic screening, whereas 37 (75.5%) had no previous screening for breast cancer. Histopathological subtypes of breast cancer were: 31 (63.3%) invasive ductal carcinoma, 10 (20.4%) mixed carcinoma, 5 (10.2%) ductular carcinoma and 3 (6.1%) lobular carcinoma.

Conclusions: Breast cancer is a very common malignancy with a 12.5% lifetime risk of occurrence. Considering women’s health as a whole, all of the women who attend to gynecology and gynecologic oncology units should be informed about breast cancer, and should be given an opportunity for breast cancer screening.
Posterior Session III

IDENTIFYING WOMEN'S KNOWLEDGE ABOUT RISK FACTORS OF BREAST CANCER AND REASONS FOR HAVING MAMMOGRAPHY

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Aim: Breast cancer is the most common cause of cancer mortality, accounting for 16% of cancer deaths in women. The aim of this study was to identify breast cancer risk factors, reasons for having mammography of the women who applied for mammography as well as to determine their level of knowledge about risk factors and level of risk perception, and anxiety concerning breast cancer.

Methods: This cross-sectional descriptive study was conducted from June 15, 2010 through September 10, 2010, in a university hospital in Ankara, Turkey. A questionnaire prepared by the researchers was used to collect the data.

Results: The mean age of the women was 52.05± 9.98 years. Sixteen percent of the women had a family history of breast cancer. The majority of participants had mammogram (75.8%) before and had gained knowledge about breast cancer and its screening (73.7%). Leading source of information about breast cancer was physicians (46.2%). Physician recommendation, screening for breast cancer, having breast-related complaints, and family history of breast cancer were important reasons to obtain mammography. The mean knowledge score about risk factors of breast cancer was 4.15± 2.73 and the mean anxiety score was 1.65±1.61. It was found that some socio-demographic and obstetrical characteristics of women, their family history, and risk perceptions about breast cancer affect their knowledge and anxiety scores about breast cancer.

Conclusion: In conclusion, the present study identified a number of factors affecting mammography participation for women. The results of this study can be helpful in promoting mammography participation in women.
Poster Session III

ROLE OF MNSOD AND IRON TRANSPORT IN STATIN-MEDIATED BREAST CANCER CELL DEATH

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HMG-CoA reductase inhibitors (statins) are FDA-approved drugs that are widely used to lower cholesterol levels in hyperlipidemic patients. Statins exert other pleotropic beneficial effects which are independent of their cholesterol lowering properties. Emerging data indicates that statins can induce cell death of variety of cancers including breast cancer cells. Earlier we have shown that statin-induced breast cancer death involves nitric oxide and arginine-dependent pathways in MCF-7 cells (Kotamraju S. et al. Cancer Res. 2007). We show that only lipophilic statins (fluvastatin and simvastatin) but not hydrophilic statins (pravastatin) induced MCF-7 and MDA-MB-231 cell death. The objective of the current study was to see whether mitochondrial component is involved in statin mediated breast cancer cell death. It was observed that both fluvastatin and simvastain dose and time-dependently increased the expression and activity of MnSOD, a major mitochondrial superoxide scavenging enzyme. This effect was correlated with a decrease in the expression of DDB2, a transcriptional negative regulator of MnSOD. Transcriptional repression of DDB2 and stimulation of MnSOD activity leading to the proapoptotic effects of statins occurred through inhibition of geranylgeranylation pathways. The antiproliferative effects of statins were coincided with a decreased expression of transferrin receptor (TfR), a major iron transport protein in cancer cells. We conclude that increased MnSOD activity and a reduction in the iron transport are in part responsible for the antiproliferative and tumoricidal effects of statin drugs.
HIGH EFFICACY OF PLATINUM COMPOUNDS IN TRIPLE NEGATIVE BREAST CANCER

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Introduction: Triple-Negative Breast Cancer (TNBC) is associated with a poor prognosis unless a pathological complete response (pCR) is achieved or almost achieved (near-pCR). There are no specific treatment guidelines for TNBC and considerably many patients fail to respond to standard anthracyclin-based chemotherapy regimens. TNBC and BRCA1-associated breast cancer are overlapping in their features to some extent and preclinical data suggest that platin analogues may act in both tumour entities.

Aim: This trial is designed to improve pCR-rates with the addition of Carboplatin to a taxane-based, anthracycline-free chemotherapy.

Methods: 31 patients with primary, unilateral, non-metastasized TNBC (majority of them cT1 or cT2, two cT3, one cT4a and one cT4b) had to be unsuitable for or refusing the standard anthracycline-based chemotherapy. They received 6 cycles, respectively in 3 cases only 5 cycles, of Carboplatin AUC 6 and Docetaxel 75 mg/m² q3w. Primary endpoint was pathological complete response (pCR) and near-pCR, secondary endpoint toxicity.

Results: 21 of 31 patients (67%) had either a pathological complete response (48%; 15/31) or a near-complete response (19%, 6/31) both being associated with a good prognosis. 9 remaining patients had a partial response, thus 97% (30/31) responded. Treatment was well tolerated - Grade III and IV toxicities were predominantly concerning neutropenia.

Conclusions: The results show a high anti-tumour activity of docetaxel and carboplatin even omitting anthracyclines in neoadjuvant chemotherapy for TNBC with good feasibility. Ongoing trials will show whether adding non-pegylated anthracyclines to weekly paclitaxel and carboplatin AUC2 will increase the pCR-rate (GEPAR-SIXTO/GermanBreastGroup).
Poster Session III

QUALITY OF LIFE IN EORTC QUESTIONNAIRES AFTER SKIN SPARING MASTECTOMY (SSM) AND IMMEDIATE IMPLANT-BASED RECONSTRUCTION WITH AND WITHOUT TITANIZED MESHES

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Introduction: The impact of immediate reconstruction on quality of life using new textured implants and titanized meshes (Tiloop Bra®) has not been evaluated by standardized quality of life questionnaires (EORTC) with regards to surgery-related morbidity and patients satisfaction.

Objective: This case cohort trial evaluates safety, aesthetic outcome and patient’s satisfaction with immediate reconstruction with and without the use of titanized mesh versus a corial flap after SSM.

Patients and methods: This large retrospective case cohort trial analysed 197 skin sparing mastectomies (SSM) in 161 patients (45 bilateral cases) and immediate breast reconstruction (IBR). We used a double-plane technique covering the implant by the submuscular pouch in its cranial half and a corial-fat-flap or titanized mesh (Tiloop bra®) for covering its lower pole or a de-epithelized corial flap in breasts with macromastia following an inferior-pedicled reduction mammoplasty pattern according to Ribeiro in the modification of Rezai.

Results: 163 women -median age of 41 years- with a total of 197 SSMs were evaluated. The majority did not experience pain and expressed satisfaction with volume, symmetry, aesthesis and quality of life in general. Partner interaction after breast reconstruction was normal. The use of titanized meshes was perceived as favourable with regards to better fitting of the breast in the bra and clothing and yielded low complication rates. The rating of patients in terms of self-perception after the reconstruction was good. Immediate reconstruction has a significant positive impact and gives the patient a considerable physical and psychological support.
Poster Session III

ENDOMETRIAL STATE IN PATIENTS WITH HORMONE-DEPENDENT BREAST CANCER

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Introduction: Breast cancer took first place in the structure of morbidity of the female population. According to the 2009 year, 61% of patients contain estrogen receptors in the primary tumor, which is the indication for hormone therapy. This therapy can induce the development of various endometrial pathologies, which is due to the dissociation of estrogen receptors in breast and endometrial tumor cells. The gold standard for hormone therapy of breast cancer is using of selective estrogen receptor modulators (SERM). There is still no consensus on the tactics of women receiving SERM. Follow-up questions remain dynamic monitoring and indications for invasive procedures, including those for diagnostic purposes are still controversial.

Material and methods: In order to prevention of development of the endometrial pathology in women with hormone-dependent breast cancer we conducted a comprehensive study of 105 patients prior to specific treatment. The average age was 48 years old. The 60.8% patients installed the I-II stage. Hormone-dependence of study was confirmed by immunohistochemical method in all cases. To study the endometrial pathology, we used clinical and anamnesis data, trasvaginal ultrasound, aspiration biopsy, hysteroscopy, fractional diagnostic curettage, followed by morphological study.

Results: 68% of the patients had the following concomitant gynecological pathology: 30% of endometrial hyperplasia, uterine cancer, in combination with adenomyosis - 36% and 2% of patients diagnosed with endometrial cancer.

Conclusions: Taking into account the adverse effects of hormone therapy on the endometrium, all patients with hormone-dependent breast cancer in need of study of the endometrium prior to treatment.
Poster Session III

EPIDEMIOLOGICAL AND PATHOLOGICAL PROFILE OF BREAST CANCER IN NIGER

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Breast cancer in Niger remains a real problem of public health in the absence of adequate and adapted health politic for their early diagnosis and their even non-existent often late care.

It is a retrospective and descriptive study led from the data of the National cancers Register of Niger country between 1992 and 2009.

The present study aims to determine and to specify the various epidemiological characteristics of breast cancers in Niger from 1992 to 2009.

During that period, 1161 cases of cancers were collected. The breast cancer represented 16.51% of all the cancers and 27.36 % of the feminine cancers collected during that the period.

The average age was 44.10±12.63 years at the woman, approximately ten years earlier than at the Arabic and European women. At the man, the average age was 49.19±13.08 years.

The majority of the patients (68.9 %) lived from Niamey area. The anatomy and cytology pathology exams allowed diagnosing 47.3 % of breast cancers. The carcinomas constituted (46.17%) the most frequent histological type. The incidence rate was 0.0023 ‰ in 1992 and 0.0110 ‰ in 2009.

The young age and stage of tumor late discovery that characterize our population are explained by the lack of awareness about breast cancer.
Poster Session III

RISK FACTORS WITH BREAST CANCER AMONG WOMEN IN IRAN: A CASE CONTROL STUDY

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Background and aim: Breast cancer is the most common malignancy in world women. The aim of this study was to find out the association of various risk factors with breast cancer among women in Guilan.

Methods and material: This was a case-control study; which was done in Razi Hospital, 2011. 351 women were studied (117 breast cancer patients and 234 control subjects). Subjects were interviewed using a questionnaire. Socio-demographic factors, socioeconomic status and, some reproductive factors were studied. X square and Odds ratio index was used for statistical data analysis.

Results: Mean age was in case (46.02), control (46.05). 80.7% cases and 80.3% controls were illiterate. There was a significant difference between cases and controls in literate (OR=1.78), occupation (OR=2.68), insurance (OR=0.38), place of residence (OR=0.34) Age at first delivery (OR=1.1) abortion (OR=2.72), menopause (OR=2.73), breast feeding (OR=0.4) and OCP (OR=0.19). While, there wasn’t a significant difference between cases and controls in marital status, menarche, co morbidity and reproductive surgery.

Conclusions: The results showed that some of socio-demographic and reproductive factors such as literate, occupation … have a significant difference with breast cancer.
Poster Session III

EVALUATION OF ENDOMETRIAL CHANGES BY TVS AND HYSTEROSCOPY IN PATIENTS TREATED WITH TAMOXIFEN FOR BREAST CANCER

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Objective: To compare transvaginal sonography (TVS) and hysteroscopy in assessing endometrial abnormalities in women on tamoxifen.

Methods: The study was carried out in 2010, in the department of obstetrics and gynaecology, B P Koirala Institute of Health Sciences, Dharan, a teaching hospital with tertiary care services in eastern Nepal for 1 year period. In a cross sectional study of 50 pre- and post-menopausal women receiving tamoxifen for > 2 years, all participants underwent TVS and EA. Those with endometrial thickness > 5 mm on TVS underwent hysteroscopy.

Results: The sensitivity and specificity when compared with histopathology as the reference standard were as follows: TVS 100% and 33.3% & hysteroscopy 92.8% and 80.8%. Prevalence of endometrial abnormalities was not significantly different in asymptomatic and symptomatic women.

Conclusion: Tamoxifen-users require routine testing for endometrial evaluation. TVS followed by hysteroscopy and biopsy is an effective option comparatively more abnormalities in the uterine cavity was noted in patients who presented with abnormal uterine bleeding.
Poster Session III

RISK FACTOR OF FIBROADENOMA AND FIBROCYSTIC DISEASE: A CASE-CONTROL STUDY
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Introduction: In a case-control study we evaluated benign breast disease associated risk factors.

Materials and methods: The study was conducted among women who attended in Iranian Center for Breast Cancer (ICBC), from 2006 to 2010.

Cases were 600 women with biopsy confirmed benign breast disease including 200 fibroadenoma and 400 fibrocystic changes. Control group were 800 women who were attended in breast clinic, without any breast-related problem in the same period of time.

Results: Mean age of attendees were 38.98 (CI 95% 39.53-38.42), 88% married, 80% educated high school and upper. There were significant differences between case and control group regarding age of full term pregnancy, use OCP and BMI.

The risk of fibroadenoma was lower in women who use of OCP than other patient odds= 0.58 (CI= 0.4- 0.8), (P< 0.0001). The age of full term pregnancy was lower in fibrocystic patients than fibroadenoma and control group (P< 0.0001). Premenopausal age was a risk factor for benign breast disease. The risk of fibroadenoma was lower in women with history of breast cancer in first degree relatives odds= 0.61 (CI= 0.43-0.88)(p< 0.008).

Conclusion: The study showed that lower BMI and use of OCP are protective factors. Premenopausal status and age of full term pregnancy are risk factors for benign breast disease. The risk of fibroadenoma decreased with increasing the history of breast cancer in first degree relatives.
Poster Session III

THE EVALUATION OF THE ENDOMETRIAL THICKNESS OF AMENORREA BREAST CANCER PATIENTS TREATED WITH TAMOXIFEN

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Background and aims: Breast cancer is one of the most common cancers in women worldwide and one of its most desirable treatments is tamoxifen. The reported side effect associated with tamoxifen is endometrial thickness and increased risk of endometrial cancer. The aim of this study was to assess the influence of tamoxifen on the endometrial thickness in amenorrhea breast cancer patients treated with tamoxifen.

Methods: This descriptive-analytic, cross-sectional study was conducted in Radiotherapy Departments of Mashhad University of Medical Sciences over a period of seven years. 162 patients treated with tamoxifen whose bleeding cycle had been disrupted were selected and the relationship between tamoxifen usage and endometrial thickness was investigated in them. In addition, the relationship between abnormal vaginal bleeding and the ultrasound findings was assessed. Data analysis was done by using t-test and Chi-square test.

Results: There was a significant relationship between tamoxifen usage and abnormal endometrial thickness while the greatest relationship was observed in the first year of treatment. The relationship between abnormal vaginal bleeding and abnormal endometrial sonographic findings was significant (P=0.001). The incidence of endometrial cancer in tamoxifen users was more than general population (0.61% vs. 0.1%).

Conclusion: Considering the findings of this study, in the presence of abnormal sonographic and clinical observations indicating abnormal vaginal bleeding, pathological evaluation of the endometrial biopsy should be carried out for patients who use tamoxifen.
**Poster Session III**

**DUPPLICATING INTERSTITIAL BREAST BRACHYTHERAPY DOSE DISTRIBUTION WITH IMRT: A DOSIMETRIC STUDY**

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**Aim:** To duplicate the dose distribution obtained from inverse planning simulated annealing (IPSA) brachytherapy with external beam intensity modulated radiotherapy (IMRT) for the boost treatment to the left sided breast carcinoma patients.

**Material and methods:** Eight previously treated patients with carcinoma of left breast were chosen and the patients were treated with 15Gy in 6 fractions brachytherapy boost after external beam radiotherapy. Flexible catheters were implanted after excision of tumors intra-operatively. By using patient CT images, lumpectomy cavity (PTV) and Organs at Risk (OAR) were contoured in Eclipse planning system (TPS). In each case, five field dynamic IMRT (6MV) plan was generated. Similarly, contoured CT data set was sent to Plato TPS and brachytherapy plans were made by using IPSA. All the plans were evaluated by using coverage index (CI=PTV\textsubscript{ref.}/V\textsubscript{PTV}) Where, PTV\textsubscript{ref.}=Volume of PTV receiving the reference dose, V\textsubscript{PTV}=Total volume of PTV. For lung and heart, volume receiving 5Gy and maximum dose (1cc volume) was noted. Radiobiological comparison is beyond the scope of this study.

**Results:**

<table>
<thead>
<tr>
<th>Indices and OAR Doses</th>
<th>IPSA</th>
<th>IMRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI</td>
<td>0.9604±0.005</td>
<td>0.9712±0.016</td>
</tr>
<tr>
<td>Lung Dose Max. (Gy)</td>
<td>11.58±3.87</td>
<td>12.76±2.59</td>
</tr>
<tr>
<td>Heart Dose Max. (Gy)</td>
<td>6.88±4.18</td>
<td>9.35±5.99</td>
</tr>
<tr>
<td>V5Gy for Lung (cc)</td>
<td>20.24±13.52</td>
<td>32.25±15.58</td>
</tr>
<tr>
<td>V5Gy for Heart (cc)</td>
<td>14.21±19.22</td>
<td>31.48±44.84</td>
</tr>
</tbody>
</table>

[Table 1]

**Conclusions:** The target coverage was comparable in both IPSA and IMRT plans. For critical structures, IPSA was better compared to external IMRT.
[Figure 1]
[Figure 2]
Poster Session III

IMPLICATIONS OF FREE RADICALS AND ANTIOXIDANT LEVELS IN CARCINOMA OF THE BREAST: A NEVER-ENDING BATTLE FOR SURVIVAL

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Introduction: Under normal circumstances, there is a balance between the oxygen derived free radicals and their destruction by the cellular antioxidant system inside the human body. However, any imbalance between the levels of these oxidants and antioxidants might cause DNA damage and may lead to cancer development.

Aim: To study was to evaluate the level of antioxidants and free radicals in blood and tissue of cancer patients and compare these levels at different TNM stages to derive the possible role of free radicals and antioxidant enzymes in the etiology of breast cancer.

Materials and methods: This study includes 30 patients suffering from cancer breast and 20 patients as controls who had benign breast diseases. Circulating lipid peroxide (Malonyldialdehyde [MDA]) levels and activities of the defensive enzymes (Superoxide Dismutase [SOD] and Catalase [CAT]) were estimated in the blood and breast tissue of these patients.

Results: Increased levels of free radicals and low levels of antioxidants were observed in malignant tissue. An elevated lipid peroxide concentration was found in the tissue of all the cancer breast patients as evidenced by an increase in the mean MDA level seen with increasing TNM stage of carcinoma breast. Levels of antioxidants SOD and CAT were decreased in cancer patients.

Conclusion: The results of our study suggest that free radical activity is enhanced in cancer breast patients while the antioxidant defense mechanism is weakened. This activity is enhanced with the increasing severity of cancer as depicted in different TNM stages of breast cancer.
Poster Session III

ENDOMETRIAL METASTASIS OF INVASIVE MIXT DUCTAL AND LOBULAR BREAST CARCINOMA, ROLE OF CYTOREDUCTIVE SURGERY IN TREATMENT. A CASE REPORT

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Introduction: The female genital tract is rarely involved by metastatic tumors. Lobular carcinoma is the most common type of breast cancer that metastasizes to the uterus. It is well-known that tamoxifen increases the risk of endometrial cancer. Although metastasis to the uterus from breast cancer is uncommon, there have been some case reports on uterine metastasis. We herein report a case in which we detected an endometrial tumor during follow-up after treatment with tamoxifen and complicated management because of the advanced disease.

Case report: We report the case of an 42-year-old female who presented with vaginal bleeding. Invasive mixt ductal and lobular breast carcinoma was diagnosed earlier and the patient received adjuvant systemic chemotherapy with adriamycin + cyclophosphamide and paclitaxel. 2 years after tamoxifen treatment, during follow up, endometrial biopsy revealed invasive mixt ductal and lobular breast carcinoma metastasis. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy. After the operation abdominal incision fistula occurred because of the ascites and intraperitoneal cisplatin was given. Subsequently liver and gastric metastasis was diagnosed and capecitabine + cyclophosphamide therapy is started.
**Conclusion:** If an endometrial abnormality is detected, the differential diagnosis of whether the uterine tumor is metastatic or primary is very important to determine the course of treatment. This case report discusses the patient’s clinical characteristics and the role of cytoreductive surgery on patient survival in breast metastasizing to the uterus. Furthermore, the metastasis to the uterus and to other organs of the genital tract can be considered as a preterminal event.
Poster Session III

LENOGRASTIM (L) VERSUS PEGFILGRASTIM (P) IN MANAGEMENT OF CHEMOTHERAPY RELATED NEUTROPENIA (CRN) IN NON METASTATIC BREAST CANCER PATIENTS (NMBCP)

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Background and aims: CRN is associated with morbidity, costs, and chemotherapy reductions. This retrospective study compared P (6 mg) with L (263 µg) to prevent CRN in NMBCP especially at first and last cycle of treatment.

Methods: 50 women (median age 54) underwent to median 6 CT doses (antracyclines+/−taxanes). At every cycle, 28 pts received daily L (5 injections from day 5 to 9), while 22 single P on day 2. Absolute neutrophil count, incidence of G3/G4-CRN, bone pain (BP: NRS>7) and cost-effectiveness were evaluated.

Results: During first and last cycle of chemotherapy, G3/G4-N was 28.5% and 11% in L, while was 23% and 0% in P. At first and last cycle of FEC100 (patients: 10 L vs 9 P) G3/G4-CRN was 20% and 0% in L, versus 22% and 0% in P. At first and last cycle of TAC/AC+T (patients: 18 L vs 13 P) G3/G4-CRN was 33% and 17% in L, versus 23% and 0% in P. Chemotherapy reduction occurred in 10 patients of L and 9 of P. Two and three Febrile-CRN (FCRN) occurred in L and P. BP was 18% in P vs 36% in L. In Italy cost of 1 P and 5 L was about 1489,00 and 655,00 euro.

Conclusions: At first cycle there is no difference between L and P respect to CRN. In TAC/AC+T P was more effective than L to prevent CRN especially at last cycle, despite major costs. No difference was found about FCRN incidence, safety and chemotherapy reduction.
Poster Session III

CORRELATION BETWEEN BMI AND CHEMOTHERAPY RELATED AMENORRHEA (CRA) IN PREMENOPAUSAL BREAST CANCER PATIENTS (PBCP)

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Background and aims: CT may induce amenorrhea to a variable extent. This side-effect may reduce fertility, cause sexual dysfunction, bone loss and menopausal symptoms. In this retrospective study we analyzed incidence of CRA in PBCP and influence of their BMI in disappearance of menstrual cycle (MC).

Methods: 24 PBCP, 43 median age years, treated with adjuvant anthracycline-cyclophosphamide (AC) and/or taxane (T). BMI was evaluated in all women. Overall population (OP) had regular MC and nobody began hormone therapy, at the same time.

Results: 10 patients received AC and 14 received TAC. In 22 patients amenorrhea appeared during CT: 90% treated with AC vs 93% with TAC. In 82% of OP amenorrhea appeared during first three cycles of CT. CRA occurred within first two doses of treatment in 14/22 patients: 66.7% treated with AC vs 62% with TAC. MC reappeared at the end of CT in 32% of patients, 40 median age years. In OP, 58% has BMI< 24.9 and 42% has BMI>25. AC: 7 patients have BMI< 24.9 (83% experienced amenorrhea) vs 3 with BMI>25 (100% experienced amenorrhea); MC reappeared in 1 pt with BMI< 24.9. TAC: 7 patients have BMI< 24.9 (86% experienced amenorrhea) vs 7 have BMI>25 (100% experienced amenorrhea); MC reappeared in 3 patients (1 with BMI< 24.9; 2 with BMI>25).

Conclusions: In our experience incidence of CRA was extremely high and there were no differences between the subgroups. MC reappeared at the end of CT in younger patients. BMI did not influence occurrence of amenorrhea.
Poster Session III

ONCOLOGIC OUTCOME OF AREOLA-SPARING MASTECTOMY WITH IMMEDIATE RECONSTRUCTION USING FREE FLAP TECHNIQUES COMPARED WITH CONVENTIONAL SKIN-SPARING MASTECTOMY

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Background: Reconstruction after breast cancer becomes increasingly important. Immediate reconstruction is an alternative to mastectomy and subsequent reconstruction. The technique of Skin sparing mastectomy (SSME) included the removal of gland, nipple areola complex. The aim of this study is to evaluate the oncological safety and technical outcomes of areola-sparing mastectomy (ASME) with immediate free flap reconstruction compared to SSME.

Methods: This retrospective analysis includes 167 patients who underwent immediate breast reconstruction using either deep inferior epigastric perforator (DIEP) flap or free transverse musculocutaneous gracilis (TMG) flap between April 2002 and September 2008. 86 patients received a DIEP flap and 81 patients a TMG flap. In 45/86 patients with TRAM flap reconstruction and in 36/81 with TMG flap reconstruction only the nipple was removed (48% ASME). We compared CR, LRR, DFS, OS and cosmetic between ASME between SSME with TRAM reconstruction.

Results: Median follow up with ASME or SSME was 5.55 years. LRR occurred in 6 (7.7\%) of 81 patients who underwent ASME and in 7 (8.3\%) of 86 patients who underwent SSME. OS in the ASME was 97.1\% versus SSME 95.2\%. No statistical differences of LRR, OS und DFS could be detected. Cosmetic outcome of ASME was better than SSME in the majority of patients.

Conclusions: Our study demonstrates that ASME with free TRAM or TMG reconstruction is as safe as SSME. Surgical removal of the areola is not associated with a lower number of local recurrences. Immediate TRAM /TMG reconstruction provides a good cosmetic outcome and patient satisfaction.
THE ROLE OF ULTRASOUND IN THE DIAGNOSIS OF GESTATIONAL TROPHOBLASTIC DISEASE

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Background: Gestational trophoblastic disease are a spectrum of trophoblastic diseases that includes: Complete molar pregnancy, Partial Molar Pregnancies, Invasive Mole, Chorioncarcinoma and Placental Site Trophoblastic tumors.

Objectives: To examine the role of sonographic findings of routine ultrasound examinations in patients with a proven histological diagnosis, postevacuation, of complete or partial hydatidiform mole.

Retrospective study:

Methods: Review of consecutive cases with a histological diagnosis of hydatidiform mole in which a pre-evacuation ultrasound examination was done. Clinical features, maternal age and gestational age were documented. Ultrasound detection rates for partial and complete hydatidiform moles were calculated and comparison of detection rates between complete and partial mole, versus gestational age groups was done.

Results: 150 consecutive cases with a diagnosis of hydatidiform mole were examined. The median maternal age was 29 (range, 15-47) years and the median gestational age was 9 (range, 5-17) weeks. According to histological diagnosis 44% were with complete moles and 56% had partial mole.

80 cases had a pre-evacuation ultrasound diagnosis suggesting hydatidiform mole 53%, including 60 complete mole and 20 partial moles, representing 40% and 13%, respectively, and 70 cases had a US diagnosis of missed abortion, blighted ovum and incomplete abortion 57%.

Ultrasound detection rate was significantly better for complete versus partial hydatidiform moles, is increased with increasing of gestational age, with an detection rate of 35-40% before 14 weeks’ gestation compared to around 60% after this gestation.

Conclusions: Routine pre-evacuation ultrasound examination identifies around 50% of hydatidiform moles, the majority sonographically appearing as missed or incomplete miscarriage. Detection rates are, however, higher for complete compared to partial moles, and improve after 14 weeks’ gestation.

Because of their higher incidence and their risk of persistent gestational trophoblastic neoplasia, early diagnosis of molar pregnancy is of clinical importance at the time of evacuation, for following up this patients and for their fertility in the future.
Poster Session III

SUBSEQUENT PREGNANCY OUTCOMES IN PATIENTS WITH MOLAR PREGNANCY AND PERSISTENT GESTATIONAL TROPHOBLASTIC NEOPLASIA

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Introduction: To evaluate the subsequent reproductive outcomes in patients with complete and partial molar pregnancy and gestational trophoblastic neoplasia (GTN) at the Motahari Hospital in Urmia- Iran from 1383-1389

Materials and methods: Questionnaires regarding subsequent pregnancies were done to all patients with history GTN were managed at the Motahari Hospital in Urmia Medical Science University.

Results: 45 patients had become pregnant after recovery, with total of 51 pregnancies. Among these, 4 were terminated by miscarriages and 3 as molar pregnancy. 36 patients had 40 term live baby delivery.

Conclusion: Patients with molar pregnancies and GTN should be reassured that they can in general expect a normal future reproductive outcome.
Poster Session III

COMPARISON OF SINGLE-AGENT METHOTREXATE AND DACTINOMYCIN IN TREATMENT OF LOW RISK GESTATIONAL TROPHOBLASTIC TUMOR

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Objective: To compare the efficacy of two different chemotherapy regimens single-agent weekly intramuscular methotrexate and every other week dactinomycin for low-risk gestational trophoblastic disease according to the FIGO staging system.

Method: From 2006 until 2010, 60 cases with low risk gestational trophoblastic tumor were diagnosed and received treatment in kosar hospital, urmia, iran. 30 patients received methotrexate weekly and 30 patients received dactinomycin every other week until documented complete response or treatment failure. We compared the number of chemotherapy courses for achieving remission, the duration of treatment, the adverse side effects, the efficacy of the treatment and the need for performing a hysterectomy among the groups.

Results: The complete remission rates were 83.3%, 93.3% for methotrexate and dactinomycin.

Drug toxicities were similar in two groups (3.3%). The duration of treatment were 43.7±24 days in dactinomycin group and 35.24±24 days in methotrexate. The courses of chemotherapy were 3.9±1.6 and 6.3±3 in dactinomycin and methotrexate groups.

Conclusion: In the management patients with low-risk metastatic gestational trophoblastic tumors, sequential single-agent chemotherapy with methotrexate and dactinomycin are similar. Dactinomycin needs less courses of chemotherapy so more acceptable for patients.
Poster Session III

PLACENTAL SITE TROPOBLASTIC TUMOR: AN OVERVIEW OF A SINGLE INSTITUTION

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To analyze 18 consecutive cases of placental site trophoblastic tumor (PSTT) treated in a single reference institution for gestational trophoblastic disease.

Consecutive patients (pts) affected by PSTT were selected from our database and retrospectively reviewed.

PSTT can develop following any type of pregnancy: in our experience the origin was a term pregnancy in 6 pts (33%), a miscarriage in 5 (28%), a termination in 2 (11%) and a molar abortion in 2 (11%), unknown previous pregnancy in 3 pts. Median age was 35 years. Median interval from last pregnancy was 13 months, but in one case even 18 years. Vaginal bleeding was present in 6 pts, in 2 amenorrhea and in one nephrotic syndrome. 17 pts underwent hysterectomy (5 following neoadjuvant chemotherapy because of partial response to medical treatment or infertility after searching for children) and one patient only medical treatment because of strong childbearing desire. First choice chemotherapy was EMA-CO regimen or EMA-EP (for refractory pts). Among chemotreated pts, two developed a metachronous tumor in the following years (one lung carcinoma and one breast cancer).

Hysterectomy represents the standard treatment, however chemosensitivity in PSTT is variable and chemotherapy alone can be considered in selected cases of young pts with strong childbearing desire.
Poster Session III

CORONARY ARTERY EMBOLIZATION OF CHORIOCARCINOMA WITH SURVIVAL

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Introduction: Choriocarcinoma is a malignant proliferation of trophoblastic tissue that tends to respond well to chemotherapy. Metastases to the lung, vagina, central nervous system, liver, and kidneys are all common in choriocarcinoma, but metastasis to the heart is rare. There have been cases of choriocarcinoma involving the heart in general, few involving coronary vessels. Survival with such metastases is extremely rare.

Case report: A 36-year-old gravida 3 para 3 previously healthy woman presented to an outside hospital seven weeks postpartum with severe chest pain and tinnitus. She experienced numerous episodes of mild, intermittent chest pain during her hospitalization, but was discharged home three days after admission on multiple cardiac medications. Two weeks later she presented to the same hospital with severe chest pain. An EKG showed changes in the inferior ST segment and T waves and cardiac enzymes were elevated. These findings were consistent with cardiac ischemia. Two days after discharge the patient was once again readmitted to the same hospital with severe chest pain. A CXR revealed multiple nodules, and subsequent MRI showed multiple masses suspicious for metastatic disease throughout the chest. Beta HCG initially 2,132,100. A transesophageal echocardiogram revealed a large mass measuring 3.0 x 0.5 cm in the left superior pulmonary vein with a tip in the left atrium and a smaller, more serpiginous mass in the right inferior pulmonary vein into the left atrium. The patient was treated with nine cycles of Chemotherapy. Response noted with Beta HCG levels returning to normal.

Conclusion: Choriocarcinoma should be in the differential diagnosis for any woman of reproductive age who presents with a myocardial infarction, especially after a recent pregnancy. This case also highlighted the importance of considering all the signs and symptoms, making a correct diagnosis, and making it early. Our patient is now 10 years disease free.
THE POSSIBILITY OF FREE β-HCG AND ITS RATIO TO PREDICT THE PROGRESSION TO GTT IN H-MOLE AND CHEMO-RESISTANCE OF GTT


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Objective: To evaluate the effectiveness of free beta human chorionic gonadotropin (free β-hCG) and its portion to total human chorionic gonadotropin to predict the group which progressed to malignant gestational trophoblastic tumor (GTT) finally in hydatidiform mole (H-mole) patients diagnosed and chemo-resistant patients groups in gestational trophoblastic tumor patients.

Materials and method: From 1995 to 2010, 196 H-mole patients and 110 persistent GTT patients were treated at CHA-GTD Center, Bundang CHA Medical center, CHA University. The value of free β-hCG was measured in our institute from 2006. 78 h-mole patients and 45 GTT patients were included. The serum total β-hCG, free β-hCG and ratio of free β-hCG/total β-hCG were measured at first as baseline value and again after evacuation 1 week later in H-mole patients and after 1 cycle of chemotherapy in GTT patients to calculate the decline ratio of these value.

Results: The ratio of free β-hCG/total β-hCG were different significantly between the H-mole group and GTT group (0.16 Vs 1.93, p< 0.05). As the predictor of progression to GTT among H-mole patients, only the decline ratio of total β-hCG at 1 week later after evacuation had significance statistically. In regard to predict the chemo-sensitive patients in GTT patients, chemo-sensitive patients had higher value of the decline ratio of total β-hCG and free β-hCG proportion compared to chemo-resistant groups (p=0.049, p=0.025)

Conclusion: The decline ratio of total β-hCG could be useful preditor both of progression to GTT group in H-mole patients and chemoresistant group in GTT patients. Also, free β-hCG proportion could be useful predictor of chemo-resistant patients among GTT patients.
Poster Session III

EPITHELIOID TROPHOBLASTIC TUMOR MIMICKING OVARIAN CANCER: A CASE REPORT

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Case report: A 59 year-old woman presented with enlarging pelvic mass for 1 month. Exploratory laparotomy revealed an 18 week-size hemorrhagic pelvic mass with dense adhesion to surrounding structures. Biopsy of the mass and omentum was performed and reported as metastatic cancer suggestive of transitional cell or squamous cell carcinoma. Neoadjuvant chemotherapy with paclitaxel and carboplatin was administered for 5 cycles with slight decrease in tumor diameter. Debulking surgery consisting of hysterectomy, bilateral salpingo-oophorectomy, omentectomy, appendectomy with partial bladder resection was performed without gross residual tumor. Pathologic report was revised as infiltrating epithelioid trophoblastic tumor (ETT) involving right parametrium, broad ligament, mesovarium and bladder wall. Similar chemotherapy was given for 6 cycles.

After a disease-free interval of 21 months the patient developed pain at right subcostal area. CT scan revealed a subcapsular hepatic nodule with splenic and peritoneal lesions. Image-guided liver biopsy was positive. The patient denied surgery. Reinduction with paclitaxel-carboplatin was given for 2 cycles then the patient developed carboplatin hypersensitivity. Single-agent paclitaxel was given for 4 more cycles before CT scan revealed enlargement of all disease sites. Chemotherapy was switched to EMA-CO regimen. CT scan every 3 cycles demonstrated gradual improvement. After 14 courses of EMA-CO the patient developed drug-induced thrombocytopenia and hepatitis. Following recovery, partial hepatectomy was performed in October 2011; the 2-cm metastatic neoplasm was removed without gross residual tumor. At present, the patient remains disease-free.

Conclusion: ETT is a rare tumor without established guideline of treatment. Report of such cases should be encouraged.
Poster Session III

ECTOPIC TUBAL CHORIOCARCINOMA: A RARE ENTITY

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Introduction: Choriocarcinoma is extremely aggressive form of gestational trophoblastic disease. The most common site of origin is uterus but can rarely be associated with ectopic pregnancy. The reported incidence of ectopic tubal choriocarcinoma is approximately 1.5 per 1,000,000 births and this is not often considered a diagnostic possibility.

Case report: We present a case of tubal choriocarcinoma diagnosed as chronic ectopic pregnancy. Serum β HCG levels which became available postoperatively were exceptionally high. At laparotomy there was a haemorrhagic, friable mass on the left side, badly adherent to bowel. Left sided salpingoopherectomy was done. Histopathology showed choriocarcinoma. She was given six cycles of chemotherapy (EMA-CO regime) and was kept under follow up by serial β HCG monitoring.

Conclusion: This case highlights the importance of histopathological examination of tubal tissue in all patients presenting with ectopic pregnancy and follow up with β HCG so as to avoid missing this rare but highly malignant but easily curable disease.
Poster Session III

CORRELATION BETWEEN POST EVACUATION HCG LEVELS AND RISK OF PERSISTENT GESTATIONAL TROPHOBLASTIC NEOPLASIA AMONG WOMEN WITH MOLAR PREGNANCIES

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Introduction: After molar evacuation women with complete hydatiform molare pregnancy are at 15 - 30% risk of persistent gestational trophoblastic neoplasia.

Objective: To develop human chorionic gonadotropin (H.C.G) criteria that determine a patient’s risk of developing persistent gestational trophoblastic neoplasia or achieving remission after molar evacuation.

Methods: In prospective study we analyze the HCG level within the third week after molar evacuation from 550 patients with molar pregnancies who Admitted in Alzahra hospital in Tabriz university of medical sciences, Tabriz, IRAN, between 2009 and 2011.

Results: Women whose h.CG level was below 150mlu/ml in the third week after evacuation had a risk of persistence below 10% but H.C.G levels above 2000 mlu/ml in the third week after evacuation was associated with 56% risk of developing persistent disease.

Conclusion: Woman with molar pregnancy who have elevated level of H.CG within the third week after evacuation are at increased risk for developing persistent disease.

These data may help clinicians to evaluate the risk of persistent diseases after molar pregnancy.
Poster Session III

COMPARING TWO TREATMENT PROTOCOLS FOR GESTATIONAL TROPHOBLASTIC DISEASE: WEEKLY SINGLE DOSE INTRAMUSCULAR AND 8-DAY INTRAVENOUS INJECTIONS OF METHOTREXATE

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Background and aim: Single agent chemotherapy with methotrexate in low and medium risk GTD has produced excellent remission rates with acceptable toxicity, cost-effectiveness and better compliance by patients. The aim of this study is to compare two treatment protocols for GTD: weekly single dose intramuscular and 8-day intravenous injections of methotrexate.

Methods: This clinical trial study was conducted in Gynecologic Oncology Department of Ghaem Hospital in Mashhad. All patients with low and medium risk GTD who required single agent chemotherapy were assigned into two groups. First group (33 patients) received IV injections of methotrexate 1 mg/m2 of body surface area and folic acid 0.1 mg/m2 every other day for 8 days; second group (14 patients) weekly single-dose IM injections of methotrexate 50 mg/m2. Two groups were matched for age, number of pregnancies, blood groups, histological characteristics and interval between end of antecedent pregnancy and start of chemotherapy. P<0.05 was considered statistically significant.

Results: Mean age of first group was 25.38±7.33 yrs and 25.7±7.52 yrs for second group. Response rates fewer than four courses of chemotherapy in first group was 45.5% and in second group 28.5% (P=0.018). 9.9% of first group and 42.1% of second group needed nearly 1.5-time increase in dose of medication (P=0.001). Requiring a change to second line of therapy from methotrexate to actinomycin D was 6.6% in first and 7.1% in second group (P=0.715). Combination chemotherapy with EMA/CO (Etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine) regimen were needed by 9.9% of patients in first and 14.2% in second group (P=0.656). Both groups achieved complete remission with no recurrence of disease.

Conclusion: Weekly single-dose intramuscular injection of methotrexate is an effective, low toxic, inexpensive and accessible method that can be performed in every center for low and medium risk GTD patients who need single agent chemotherapy.
Poster Session III

PRIMARY MANAGEMENT OF "INTERMEDIATE RISK" DISEASE. HAVE WE MADE A MISTAKE?

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Patients with persistent trophoblastic disease, and a W.H.O. risk score of 5 or 6 have been primarily treated with a single drug "low risk disease" regimen since the 2002 changes to the F.I.G.O. staging system and the W.H.O. risk score. Evidence from several phase III trials and from at least 3 large single institution datasets strongly suggest that these patients have a significantly lower rate of primary cure with first-line single agent therapy. Data will be presented to demonstrate that, although the primary response rate with patients who have risk score of 0 - 4 is in the order of 80 percent, the success of first-line single agent treatment with risk score 5 and 6 is less than 50 percent. It is recommended that these patients with so-called intermediate risk disease be treated with a more intensive regimen because it has been previously shown that a change in treatment regimen is psychologically very difficult for these generally young, reproductive-aged women.
Poster Session III

RESULTS OF SALVAGE CHEMOTHERAPY FOR PATIENTS WITH RELAPSED OR RESISTANT GESTATIONAL TROPHOBLASTIC NEOPLASM


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Background: In spite of the high survival rate of gestational trophoblastic neoplasm (GTN) patients with combination chemotherapy, etoposide-methotrexate-actinomycin D/cyclophosphamide-vincristine (EMA/CO) failures are reported in up to 15% of high-risk patients. As a salvage therapy, various regimens have been used including etoposide-methotrexate-actinomycin D/etoposide-cisplatin (EMA/EP). Recently several reports suggest that paclitaxel-containing regimens also have activity in refractory GTN.

Aims: We evaluated the effectiveness and toxicity of paclitaxel-etoposide/paclitaxel-cisplatin (TE/TP) or EMA/EP to salvage women who were heavily treated for GTN.

Methods: Total ten patients were included for this retrospective study, who had progressed on or relapsed from EMA/CO and received no prior cisplatin-based regimens. As a salvage therapy regimen, TE/TP had been used for seven patients, EMA/EP for two and both for one.

Results: A median follow-up period was 19 (range 3-132) months. Six (60%) patients achieved a complete response (CR) and three (30%) a partial response. One patient progressed on both EMA/EP and TE/TP. Overall survival rate was 40% in that four CR patients remained alive at reporting for 5, 48, 60, and 132 months respectively, two of whom came from EMA/EP. Adverse events over grade 3 or 4 were as follows: neutropenia (90%), anemia (50%), thrombocytopenia (20%), and nausea or vomiting (20%).

Conclusion: TE/TP or EMA/EP can be an effective and tolerable treatment to salvage patients failing EMA/CO. Large studies are needed to validate these results. Furthermore a comparative study can suggest more feasible regimen especially in context of toxicity considering relatively high incidence of adverse events.
PRIMARY CHORIOCARCINOMA OF THE OVARY WITH CEREBRAL METASTASIS MIMICKING AN ECTOPIC PREGNANCY - A CAUTIONARY TALE?

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Background: Choriocarcinoma of the ovary, either gestational or non gestational in origin is a rare entity. Preoperative diagnosis is difficult especially in young women due to non specific clinical symptoms.

Case: A 30 year old G5P2L2A2 presented with 2 months amenorrhoea and spotting per vaginum for 2 days. Urine test for hCG was positive and ultrasound revealed a normal uterus and a left complex adnexal mass measuring 8×6 cms. A provisional diagnosis of ectopic pregnancy was made. On laparotomy, the left ovary was replaced by a solid vascular mass densely adherent to the sigmoid colon. (Figure 1)

[Figure 1]

Left salpingoovariotomy was carried out with difficulty after releasing the adhesions. On the second postoperative day, she developed headache and vomiting. Fundus examination showed papilloedema and CT scan revealed 2 metastatic deposits in the parietal and temporal lobes. Choriocarcinoma was suspected, serum βhCG was 72,000 IU/ml, CXR showed a 2cm lesion in the right lower lobe and histopathology revealed ovarian choriocarcinoma. She was being managed with anticerebral oedema measures and chemoradiation but her condition deteriorated and she was taken home against medical advice.

Conclusion: A high index of suspicion for choriocarcinoma is necessary in a young patient with amenorrhoea and a complex adnexal mass. Estimation of serum βhCG plays a key role in the management.[HP1] In a patient of choriocarcinoma with cerebral involvement, multidisciplinary team
of surgical, medical and radiation oncologist along with gynaecologist is needed to provide optimal care.
Poster Session III

CHORIOCARCINOMA FOLLOWING TERM PREGNANCY

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Background: Gestational choriocarcinoma is an aggressive infiltrative malignancy and occurrence after a term pregnancy is uncommon. It is fraught with a high frequency of missed or delayed diagnosis and late hospital presentation in affected females.

Materials and method: Tissue biopsies were fixed in 10% formalin, processed in paraffin and stained with haematoxylin & eosin.

Results: 57 histologically confirmed choriocarcinoma cases were seen over a 12 year period. Of these, 6 had metastatic involvement of the cervix, vagina, vulva, fallopian tube and face. One of the metastatic cases is a 37 years old multiparous female who presented with 9 months history of persistent vaginal bleeding post delivery of a term baby. Initial manual vacuum aspiration (MVA) revealed retained products of conception, however, test for bHCG was positive in neat and 1:200 dilution. A histopathological diagnosis of choriocarcinoma was established after the 4th MVA. She also had emergency total abdominal hysterectomy secondary to torrential uncontrollable vaginal bleeding and biopsied tissues from the specimen were consistent with choriocarcinoma. She was commenced on combination chemotherapy but re-presented 5 months later with a mediastinal mass, severe chest pain, cough and blood streaked sputum. Chest X-ray revealed cannon balls within the lung parenchyma while biopsy from the mass showed a metastatic choriocarcinoma. She died shortly before of further chemotherapy.

Conclusion: Gestational choriocarcinoma is completely curable when therapy is instituted early. Histopathological analysis of dilation and curettage specimen and HCG monitoring should forestall delayed diagnosis thus reducing the high morbidity and mortality of this disease. Wide spread metastasis affect over all prognosis and survival.
Poster Session III

THE EXPRESSION AND CLINICAL SIGNIFICANCE OF MASPIN, P53 AND C-ERBB-2 IN GESTATIONAL TROPHOBLASTIC DISEASE

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Objects: To analyze the expressions and potential association of maspin, p53 and c-erbB-2 in gestational trophoblastic disease, and their relationship with malignant high risk factors.

Methods: The protein expression of maspin, p53 and c-erbB-2 were detected in 24 cases of normal early pregnancy, 88 cases of hydatidiform moles (39 progressed to gestational trophoblastic tumors, GTT) and 11 cases of GTT by immunohistochemistry.

Results: The expression of maspin was significantly lower in hydatidiform mole and GTT than it in normal early pregnancy (P=0.016, P< 0.001). The expression of maspin was significantly lower in GTT than it in hydatidiform mole without malignant transformation (P=0.001). The expression of p53 was significantly higher in hydatidiform mole and GTT than it in normal early pregnancy (P=0.031, P< 0.001). The expression of p53 was significantly higher in GTT than it in hydatidiform mole without malignant transformation (P=0.016). There were significant difference of maspin (P=0.006) and P53 (P=0.009) between hydatidiform mole with and without malignant transformation. The expression of c-erbB-2 was significantly higher in hydatidiform mole with malignant transformation and GTTs than it in normal early pregnancy (P=0.009, P=0.027). The expression of c-erbB-2 was significantly higher in GTTs than it in hydatidiform mole without malignant transformation (P=0.048). In moles with malignant high risk factors (HCG>100,000U/L, uterus volume> gestation weeks, ovary lmein cyst >6cm), the expression of maspin was lower than those without risk factors groups (P< 0.001, P < 0.001, P=0.006), while the expression of p53 was significantly higher than that without malignant high risk factors (P=0.006, p=0.023, p=0.012). The expression of c-erbB-2 in hydatidiform mole with risk factors that uterus volume> gestation weeks was higher than in those without risk factors (P=0.005).
Poster Session III

GESTATIONAL TROPHOBLASTIC NEOPLASIA AND HIV INFECTION: A 10-YEAR REVIEW

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Objectives: To describe the management of Gestational Trophoblastic Neoplasia, with particular reference to concurrent HIV infection.

Methods: Retrospective descriptive study of all cases of GTN managed at Groote Schuur Hospital over a 10-year period (1999-2008).

Results: Seventy-six patients were included in the study with a median age of 30 at presentation. Only 36 (47.4%) patients had known HIV status. Fourteen (18.4%) were HIV-Positive and of these, 4 (28.6%) were on anti-retroviral treatment (ARV). The mean CD4 count was 142 cells/microl for those on ARV and 543 cells/microl for those not on ARV (p = 0.001). Histologically, 44 (58%) patients had hydatidiform mole and 21 (28%) had choriocarcinoma. In the remaining 10 cases, a clinical diagnosis was made. Based on the revised FIGO/modified WHO Scoring, 43 (56.6%) patients were low risk and 33 (43.4%) were high risk. Thirty-eight (50%) patients were staged as FIGO Stage 1. Of 73 patients who received chemotherapy, 56 (76.7%) achieved complete remission, 9 (12.3%) did not achieve any remission, 7 (9.6%) had a relapse and 1 (1.4%) was lost to follow-up. Patients who never went into remission had frequent treatment delays due to poor compliance or inadequate blood counts. The overall survival at 60 months was 81.9%. Of the 13 (17.1%) patients who have died, 5 (38.5%) were HIV-Positive. The overall 5-year survival for FIGO Stage I, II, III and IV were 97.4%, 66.7%, 77.8% and 46.2%, respectively. The overall 5-year survival for HIV-Positive patients was 64.3% versus more than 85% for both the HIV-Negative and HIV-Unknown groups.

Conclusions: Apart from more advanced stage, HIV seropositivity and poor compliance with treatment also portend poorer outcome in GTN patients. In HIV-Positive patients with poor CD4, little clarity is available whether ARV should be commenced speedily and the administration of chemotherapy delayed until immune reconstitution occurs.
COLOR DOPPLER SONOGRAPHY CAPABILITIES IN TROPHOBLASTIC TUMOURS

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Objective: To assess the ultrasound characteristics of hydatidiform mole and postmolar malignant trophoblastic tumours

Methods: Examined 351 patients. The mean age was 31±2.4 year (range from 17 to 44). Survey was carried out on the device SONOScape SSI-1000 by sensors of 6-2 MHz (transabdominally) and 9-5 MHz (transvaginally). Tumour nodes in a uterus are revealed at 28 patients (7.98%). Based on hCG regression curves postmolar malignant trophoblastic tumours were diagnosed in 11 patients (3.13%). All patients with malignant trophoblastic tumours have been tumour nodes in myometrium.

Results: Trophoblastic nodes were diagnosed: in a uterine cavity - in 9 (32%) patients, in myometrium - in 19 (68%). The mean sizes of nodes in a cavity was 28±2.3 mm (range from 20 to 40 mm) with prevalence of solid and cystic type - in 5 (55%). In most cases at Color Doppler sonography were detected mixed type of a blood-groove (45%). The mean sizes of nodes in myometrium was 34±5.2 mm (range from 10 to 60 mm), with prevalence of solid type - in 13 (68.4%) women. The most frequent localization - in the rear wall of the uterus (42.1%); blood flow in the periphery of the tumor node in 52.6% cases.

Conclusion:

1. Ultrasound second largest (after hCG) screening method in the diagnosis of trophoblastic tumors.

2. Color Doppler sonography affords detection areas of abnormal blood flow within the uterus.
Poster Session III

LOW VALUE OF PET/CT IN PREDICTION OF LYMPH NODE METASTASIS OF EARLY STAGE CERVICAL CANCER

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Objective: The value of PET/CT in predicting lymph node involvement of early stage cervical cancer is not well determined. The aim of our retrospective study is to investigate of clinical value of PET/CT in primary lymph node staging of FIGO stage IA2-IIA cervical cancer.

Method: We collected thirty six patients with early FIGO stage IA2-IIA cervical cancer performed preoperative PET/CT scan and radical hysterectomy with pelvic (or paraaortic) lymphadenectomy. The PET/CT findings of each patients were compared to postoperative pathologic findings.

Results: Lymph node metastasis was confirmed in seven patients (19.4%), two of these had FDG uptake in the pelvis on PET/CT scan. only two were true positive. In twenty-nine patients without lymph node metastasis, twenty six had true negative PET/CT scans concerning pelvic lymph nodes. We found the positive predictive value (PPV) to be 40%, negative predictive value (NPV) 83.8%, sensitivity 28.5%, specificity 89.6%.

Conclusion: Preoperative PET/CT scan in early stage cervical cancer has low clinical value for prediction of lymph node metastasis. We need large sample-sized prospective trial to verify clinical value of preoperative PET/CT.
Poster Session III

ASSESSING THE BENIGN WORKLOAD OF A GYNAECOLOGICAL ONCOLOGIST

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Background: Preoperative identification of malignancy is crucial for efficient management planning in treating female genital tract cancers. This study analysed the case mix, by post-operative Histology criteria, on a dedicated Gynaecological oncology list over a 112 month period at a UK Cancer Centre.

Method: We conducted a retrospective study from October 2002 to January 2012. Preoperatively identified benign cases were excluded. Clinical findings, imaging, biopsy histology and RMI were utilized by a Multi-Disciplinary Team to categorize lesions as malignant. The final histology report was then analysed for comparison.

Results: A total of 949 cases were identified. In these patients, malignancy was confirmed in 744 (78.4%). 205 (21.6%) had benign histology. More than half (486) of the total patients had surgery for ovarian pathology and of these only 65% (314) were histologically malignant. 290 cases had endometrial pathology and 92% (267) of them were malignant. Many of the benign cases were endometriotic or complex myomas.

Conclusions: We have demonstrated that, despite careful pre-operative triage, a significant part of a dedicated gynaecological Cancer list involves benign cases. With Ovarian mass cases in particular, improved modalities of imaging and tumour marker assessment are required. Use of the International Ovarian Tumour Analysis (IOTA) group protocol may improve accuracy.
Poster Session III

TISSUE AUTOFLUORESCENCE AND A P53 TARGETING MOLECULAR PROBE: NOVEL APPROACH FOR THE DETECTION OF EARLY TUBAL INTRAEPITHELIAL CARCINOMA

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Background: Tubal intraepithelial carcinoma (TIC) sites in fallopian tubes (FT), the majority of which are p53 positive, are understood to be precursor lesions to high grade serous carcinoma (HGSC) of the ovary. Cancerous and precancerous changes in epithelium lead to loss of normal tissue autofluorescence (AF), imaging that detects alterations in light-activated endogenous fluorescence properties of tissue, enabling real-time, high resolution imaging. This approach is effective in detecting precancerous lesions in the lung, oesophagus, colon, oral cavity, and cervix. Preliminary studies indicate that abnormal FT lesions can also be detected using this imaging technique.

Aim: We sought to apply optical imaging technology assessing tissue AF to define TIC lesions in resected FTs from patients at high risk of developing HGSC.

Results: Regions identified with a loss of AF in ex vivo FTs yielded a high rate of concordance with histopathologic assessment. In parallel, a fluorescently labeled molecular probe targeting intracellular p53 has been developed and shows high specificity when tested in cell and tissue models.

Conclusion: The use of optical imaging for AF and molecular staining for p53 is a novel and promising approach to detect and verify the presence of TIC lesions in fallopian tubes. Given the absence of effective screening approaches for earlier detection of this disease, our combined approach has the potential to significantly improve management approaches in patients with a high risk of disease and positively impact survival outcomes.
Poster Session III

PYOMETRA: AN UNSUAL FINDING ASSOCIATED WITH MALIGNANCY: REPORT OF EIGHT CASES

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Introduction: Pyometra an unusual finding in gynecologic practice is the accumulation of exudate in uterine cavity arising from obstructed cervical passage. It is usually associated with genital malignancy particularly cervical cancer in postmenopausal women.

Materials and methods: Demographic and histopathologic characteristics of eight women presenting with signs and symptoms of pyometra admitting to gynecologic oncology unit was evaluated in two years period.

Results: There were 8 women presenting with pyometra. Median age was 74 years. All but one women presented with foul smelling vaginal discharge. One patient had severe crampy pelvic pain. Ultrasonography revealed retention of fluid in endometrial cavity in 6 patients. Two patients had sonographically irregular endometrial thickness. Three patients were diabetic and 6 had hypertension. Two women could not be operated because of accompanying disease (advanced congestive heart failure and acute pulmonary embolism). One of these two women had endometrial carcinoma and the other had benign findings in endometrial sampling.

Six out of eight women revealed genital malignancy. There were three women with endometrial carcinoma, two with cervical carcinoma and one patient with immature teratoma. Two women with postoperative diagnosis of cervical cancer had normal preoperative cervical cytology and endometritis in endometrial pathology. Two out of three patients with endometrial carcinoma had stage I disease. Two patients with cervical cancer had stage I disease.

Conclusion: Malignancy should be ruled out particularly in postmenopausal women presenting with pyometra even if cervical cytology and endometrial biopsy reveal benign findings.
Poster Session III

THE ACCURACY OF PET/CT IN DETECTING PARA-AORTIC MICROMETASTASES IN LOCALLY ADVANCED CERVICAL CANCER COMPARED WITH LAPAROSCOPIC PARA-AORTIC NODE DISSECTION

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Introduction: PET/CT offers advantages over other imaging modalities in the assessment of para-aortic nodal disease and the detection of distant metastasis. In our institution we used PET/CT to evaluate extra-pelvic disease prior to undertaking Laparoscopic Extra-peritoneal Para-Aortic Node Dissection (LEPAND). Para-aortic node involvement is an important prognostic indicator for women for cervical cancer. Detection allows tailoring of radiotherapy fields prior to the administration of chemo-radiotherapy.

Objectives: The primary aim of this study was to determine the accuracy of PET/CT in detecting para-aortic node micro-metastases in cervical cancer.

Patient and methods: All women in Northern Ireland were treated in the Northern Ireland Cancer Centre. PET/CT was performed in women with FIGO Stage IB2 to IVA cervical cancer prior to undergoing LEPAND and then chemo-radiotherapy from 2010 to 2012. All women underwent clinical staging and a MRI scan prior to PET/CT and treatment. All the PET/CT were performed in a single unit and reported by a dedicated group of Consultant Radiologists with a special interest in PET/CT.

Results: We report the accuracy, sensitivity and specificity for PET/CT in apparent locally advanced cervical cancer compared with the gold standard, laparoscopic para aortic nodal dissection.
Poster Session III

THE COMPARISON OF THE EFFECTIVENESS OF BIOPSY COMBINED WITH HYSTEROSCOPY AND DILATATION AND CURETTAGE FOR THE DETECTION OF ENDOMETRIAL PATHOLOGIES

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Background and aims: Approximately 33% of all females are referred to gynecology clinics with abnormal uterine bleeding. Currently, biopsy combined with diagnostic hysteroscopy and dilatation and curettages (D&C) are the most common used methods in the diagnosis of patients with abnormal uterine bleeding. The aim of this study is to compare the effectiveness of biopsy combined hysteroscopy and D&C in the diagnosis of endometrial pathologies.

Methods: This study was performed at the Department of Obstetrics and Gynecology of university hospital between December 2010 and July 2011. A total of 83 patients, who have admitted with abnormal uterine bleeding and underwent biopsy combined with hysteroscopy and D&C, were included to this prospective study.

Results: Histopathological results were as follows: endometrial polyps in 40 (48%) patients, endometrial hyperplasia in 11 patients (13%), endometrial cancer in 4 patients (4.8%), submucous myoma in 4 patients (4.8%) and normal endometrial tissue in 24 patients (28.9%). The sensitivity, specificity, positive and negative predictive values of biopsy combined with hysteroscopy were 90.1%, 100%, 100% and 78.5% respectively. The corresponding values for dilatation curettages were 67.2%, 34.9%, 100%, and 52.3% respectively.

Conclusions: Althought biopsy combined with hysteroscopy seems to be superior to D&C for the investigation of patients with abnormal uterine bleeding, none of them is completely enough for detecting endometrial pathologies alonely. We conclude that the use of these methods together will provide more accurate results in diagnosis and treatment of endometrial pathologies.
Poster Session III

DOES LYMPHADENECTOMY PERFORMED IN GENITAL CANCERS EFFECT BODY FLUID COMPOSITION? A PROSPECTIVE STUDY

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Introduction: Lymphadenectomy is an essential part of staging procedure of female genital cancers but morbidity related to lymphadenectomy is a concern particularly for women with accompanying chronic diseases. We assessed changes in body fluids and bioimpedance markers in women undergoing systematic pelvic paraaortic lymphadenectomy by bioimpedance measurements.

Materials and methods: We prospectively evaluated changes in body fluid composition in different compartments by using bioelectrical impedance (BIA). Parameters including Total (TBW), extracellular (EBW) and intracellular body water (IBW), phaseangle, reactance, illness marker were evaluated preoperatively and 1 week after staging surgery and in control group including patients undergoing surgery for benign reasons.

Results: 150 women were included. 64 % was operated for benign pathologies and 36 % had genital cancers and subjected to pelvic and paraaortic lymphadenectomy. Mean age for patients with benign pathologies and malignant pathologies were 45 (range 20-75) and 56 (21-82) years respectively. 50 % of patients with malignant pathologies had endometrial, 33 % had ovarian and 13 % had cervical carcinoma. Mean retrieved lymph nodes were 30 and 8 for pelvic and paraaortic region respectively. Regarding body fluid changes there were no difference in preoperative and postoperative measurements of TBW (p= 0.64 and 0.06), IBW (p=0.82 and 0.07), EBW (p=0.21 and 0.07) phaseangle (p=0.70 and 0.79), reactance (p=0.33 and 0.44) and illness marker (p=0.43 and 0.07) both in malignant and benign patient populations respectively.

Conclusion: Pelvic and paraaortic lymphadenectomy does not lead to significant changes in distribution of body fluids.
HIGH SENSITIVITY AND SPECIFICITY USING PET/CT AND LAPAROSCOPIC DIAGNOSTIC EXCISION TO VERIFY LYMPH NODE METASTASES IN CERVICAL CANCER PATIENTS

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Purpose: The purpose of the current study was to evaluate PET/CT verifications of laparoscopic diagnostic lymph node excision, detecting lymph node (LN) metastasis in cervical cancer patients.

Material and methods: Single institution retrospective analysis of procedure efficacy and survival in cervical cancer patients with PET/CT positive LN.

Patient inclusion criteria: Histopathological diagnosis of cervical cancer, LN metastases at PET/CT prior to staging, laparoscopic diagnostic LN excision, control PET/CT after surgery.

A Missed Lesion (ML) was a lesion seen on the staging PET/CT with no sign of tumor tissue at histological analysis and a subsequent planning PET/CT revealing the same lesion as before laparoscopy.

Kaplan Meier plots and log-rank tests were performed.

Results: 65 patients were included. Laparoscopy confirmed metastatic LN in 39 patients. In 4 of 26 patients with negative laparoscopic results, the control PET/CT showed ML. Of these, 3 patients were re-operated of which 2 had LN metastases confirmed, and 1 continued having still no evidence of metastatic disease (Figure 1).

Of the total 23 patients with twice verified negative LN pathology, 1 patient died. Of the 42 patients with metastases, 15 died.

For the entire staging procedure sensitivity and specificity were 0.98 and 1.00 respectively. Positive and negative predictive values were 1.00 and 0.96.
Conclusions: Using PET/CT as control of laparoscopic diagnostic lymph node excision provides both high sensitivity, specificity as well as high positive and negative predictive values, for the staging of lymph node metastases in cervical cancer patients.
Poster Session III

IS THE FIGO2008 STAGING OF ENDOMETRIAL CANCER MORE ACCURATELY CORRELATED TO PROGNOSIS?


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Objectives: We retrospectively analyzed clinical prognosis and its correlation with both the FIGO2008 and the FIGO1988 staging system.

Patients and methods: In this study, we analyzed 1134 patients who were diagnosed with endometrial cancer and received treatment including hysterectomy from 1990 to 2010 at our institution. The patients were classified using both FIGO2008 and FIGO1988 based on the information of the pathological diagnosis. We analyzed the correlation between surgical staging and prognosis for both staging systems.

Results: Compared to FIGO1988, there was an increase of 71 patients in stage I cases, a decrease of 37 patients in stage II cases, and a decrease of 38 patients in stage III cases with FIGO2008. The subclassification of stage I and II with FIGO2008 more accurately reflected PFS and OS compared to FIGO1988. However, there was no difference in PFS and OS for the subclassification of stage IIIc cases. Stage IIic1 patients without paraaortic lymphadenectomy had significantly poorer prognosis compared with patients who underwent paraaortic lymphadenectomy. However, if the patients who did not undergo paraaortic lymphadenectomy were excluded, the patients in stage IIic1 tended to have better OS compared to stage IIic2.

Conclusions: This study demonstrates that FIGO2008 is more accurately correlated to prognosis in stage I and II patients compared to the FIGO1988. However, this study also revealed that it is difficult to correctly designate the staging of patients who did not undergo paraaortic lymphadenectomy when evaluating prognosis in subclassification of stage IIic cases.
AUDIT ON THE USE OF PET/CT IN THE MANAGEMENT OF CERVICAL CANCER

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Introduction: Cervical cancer (CC) is a significant cause of death and one of the most frequent cancers in women worldwide. CC is staged using FIGO criteria - clinical staging not taking into account complex imaging modalities such as CT, MRI or PET/CT. Efforts to accurately assess primary tumour and confirm absence of nodal involvement is necessary as up to 36% of cases present with nodal disease. Management of early stage CC is usually surgical and confers a good prognosis with an improved side-effect profile compared to radiotherapy (RT) or chemo-radiotherapy (CRT). A subset will require CRT following surgery. For these patients outcome for disease control and overall survival is the same as using CRT alone but morbidity of tri-modal treatment is much higher, with greatly increased risk of complications such as lymphoedema or fistula formation. A higher sensitivity for PET/CT in detecting metastatic lymphadenopathy has been reported thus raising the potential to significantly change management, avoiding surgery in many cases.

Materials and methods: A prospective data collection of 26 consecutive women with Stage 1B1 CC.

Results: In 50% of cases PET/CT provided information not seen on original imaging (4% hydronephrosis, 31% nodal metastases, 15% distant metastases), 31% patients had additional RT, 8% additional surgery and 11% changed to palliative strategy. 1 patient (4%) had a false negative PET/CT with microscopic LN metastases seen on subsequent lymphadenectomy.

Conclusion: PET/CT changed management in our patients with CC and should be considered a routine investigation prior to surgery or radiotherapy. A bigger multi-centre study is currently planned to investigate this further.
SAFETY AND ACCURACY OF CO2 HYSTEROSCOPY IN ASSESSING CERVICAL INVASION BY ENDOMETRIAL CARCINOMA: COMPARISON WITH TRANSVAGINAL SONOGRAPHY AND MRI

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Objectives: To compare the reliability of diagnostic carbon dioxide hysteroscopy, transvaginal sonography (TVS) and magnetic resonance imaging (MRI) in the pre-operative evaluation of cervical involvement by endometrial carcinoma.

Materials and methods: A prospective study was conducted on 100 patients with histological diagnosis of endometrial carcinoma. Prior to definitive surgical treatment, all patients underwent diagnostic carbon dioxide hysteroscopy, TVS and MRI. Results were compared with pathological examination on surgical specimen. The sensitivity, the specificity, the positive and negative predictive values and the accuracy of the three techniques for recognizing the cervical involvement by the carcinoma were calculated.

Results: The specificity of TVS (0.96), RMI (0.96) and hysteroscopy (0.93) were similar, while RMI had a sensibility (0.66) higher than TVS (0.44) and hysteroscopy (0.33). Compared to TVS and MRI, hysteroscopy showed the highest negative predictive value (0.39, 0.38 and 0.66 respectively), while RMI the highest positive predictive value (0.57, 0.66. and 0.37 respectively).

Concerning the diagnostic accuracy, TVS (0.89), RMI (0.89) and hysteroscopy (0.89) had similar values. As regard as peritoneal cytology, only three patients were positive and interestingly all three had serous histology.

Conclusions: This study demonstrates that hysteroscopy is more accurate than MRI and TVS in assessing the exclusion of cervical canal involvement in patients with endometrial carcinoma, whereas MRI is the most reliable technique for predicting cervical involvement.

In conclusion carbon dioxide hysteroscopy and MRI are both useful in the preoperative staging of endometrial carcinoma in order to plan the correct surgical strategy.
DIAGNOSTIC ACCURACY OF MRI IN ENDOMETRIAL CANCER


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Background and aims: MRI assessment of endometrial cancer is increasingly accepted as standard practice within the UK; there is lack of quality data to support the accuracy and clinical usefulness of this practice. This study investigated the accuracy and clinical application of MRI in the surgical planning of endometrial cancer.

Methods: Prospective diagnostic accuracy study of pre-operative MRI findings and hysterectomy specimens with respect to depth of myometrial invasion. The impact of MRI added to pre-operative biopsy tumour grade to predict disease necessitating full staging was calculated.

Results: The sensitivity of MRI for detection of outer half myometrial invasion was 0.73 (95% CI 0.59 to 0.83) and specificity 0.83 (95% CI 0.76 to 0.89). Positive predictive value was 0.63 (95% CI 0.50 to 0.74) and negative predictive value 0.89 (95% CI 0.82 to 0.93).

Sensitivity of endometrial biopsy grade predicting necessity for full staging was 0.65 (95% CI = 0.54-0.75) and rose to 0.73 (95% CI 0.62-0.81) when MRI analysis of disease spread outside the body of uterus was added to the triage process. Specificity of endometrial biopsy in identifying extra-uterine spread decreases from 0.97 (95% CI = 0.92-0.99) to 0.86 (95% CI = 0.78-0.92) with the addition of MRI.

Conclusions: Pre-operative MRI is a moderately sensitive and specific method of identifying endometrial cancer invasion involving the outer half of the myometrium. The sensitivity and negative predictive value of pre-operative tumour grade as an indication for full surgical staging improves when MRI is added to the pre-operative assessment process.
Poster Session III

RADIOLOGIC IMAGING PATTERNS OF GYNECOLOGIC PATIENTS: DOES PHYSICIAN SPECIALTY MATTER?

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Objective: To study the patterns of imaging by gynecologists and non-gynecologists (family physicians and others) following a pelvic ultrasound in women aged 45 and older, prior to a surgical intervention.

Methods: Provincial databases of health care utilization were linked to establish patterns of imaging and surgical outcomes between 2006 and 2008. Women 45 and older without any surgical or imaging history met the inclusion criteria for this study.

Results: 193,261 women met the inclusion/exclusion criteria; of those, 19,125 underwent a laparotomy. 18,632 women underwent surgery for a gynecologic indication. 87% of women had imaging initiated by a non-gynecologist with the remainder initially imaged by a gynecologist. Comparing percentages of further imaging incurred by patients as categorized by initial imaging physician, non-gynecologist vs. gynecologist, additional imaging differed as follows: repeat pelvic ultrasound 42% vs. 24%; abdominal ultrasound 30% vs. 12%; CT abdomen/pelvis 13% vs. 4%; MRI pelvis 4% vs. 1.5%. Time to surgery also increased in malignant cases based on imaging ordered: uterine malignancy mean time to surgery with pelvic ultrasound alone was 138 days vs. 213 days when CT scan and MRI was ordered; for malignant adnexal disease time to surgery increased from 100 days to 180 days (p< 0.001).

Conclusion: There is an important discrepancy between gynecologists and non-gynecologists with regards to patterns of imaging involving gynecologic pelvic pathology. Educational interventions are needed to reduce potentially unnecessary imaging tests, which lead to treatment delay of serious underlying conditions including cancer.
Poster Session III

SENTINEL NODES BIOPSY CAN ACCURATELY PREDICT LYMPH NODES METASTASES IN EARLY STAGE CERVICAL CANCER, COMPARED WITH MRI AND PET-CT


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Objective: To describe the usefulness of lymphatic mapping and sentinel lymph nodes (SLNs) biopsy in early stage cervical cancer compared with MRI and PET-CT.

Method: Patients diagnosed with cervical cancer at the early stage (FIGO Ia2~Ib1) were included. They were underwent FDG PET/CT and MRI before surgery. 99mTc-labeled phytate and patent blue dye were used to detect SLNs. We identify SLNs and submitted to fast frozen section. Patients who desired pregnancy and their SLNs were negative metastasis on frozen section underwent fertility sparing surgery: radical trachelectomy (RT).

Results: In 28 months, 44 patients were included. The SLNs detection rate was 86%. SLNs of 4 patients who weren't pointed out metastasis by MRI or PET-CT were positive on frozen section. Therefore those patients had to undergo radical hysterectomy. On the contrary, one patient who was suspected lymph nodes metastases by PET-CT was negative on frozen section and we could perform RT.

Conclusion: Lymphatic mapping and SLNs biopsy can more accurately predict lymph nodes metastases in early stage cervical cancer, compared with MRI and PET-CT. This procedure may help select patients who would benefit from such fertility-sparing surgery.
INITIAL NODAL STAGING OF LOCALLY ADVANCED CERVICAL CANCER WITH FDG-PET

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Objective: To evaluate the reliability and useful of FDG-PET/CT for primary para-aortic nodal staging of locally advanced cervical cancer (LACC).

Methods: This prospective study included 21 women (25-78 years old; mean age = 53.3) diagnosed with LACC. All patients underwent a whole-body FDG-PET/CT for primary staging. PET positive findings were described (site, maximum diameter and SUVmax) and correlated with MRI results, follow-up and histopathology including surgical exploration for para-aortic lymphadenectomy (PAL) by laparoscopic preperitoneal approach.

Results: All cases were squamous cell carcinoma. FIGO stage was: IB2 (4), II (14), III (3) and IV (1). All the primary tumours showed FDG uptake (SUVmax=8-36; mean 15,5).

MRI was performed in 20/21 and parametrial involvement was found in 18/20.

FDG-PET/CT showed positive para-aortic nodes in 4 patients: 3 TP (1 with a positive PAL and 2 with confirmed extraabdominal metastasis) and 1 FP with a negative PAL.

PAL was technically feasible in 15/22 women: positive in 2 (1 TP and 1 FN by PET) and negative in 11 (10 TN and 1 FP by PET). NPV was 90%.

The treatment was modified in 3/21 (13%) women that received chemotherapy because of detection of unsuspected distant metastasis.

Conclusion: This pilot study suggests that PET/CT is an effective imaging technique in the initial staging of LACC. It may help to evaluate para-aortic nodal metastasis and to plan the management, especially when unsuspected distant metastases are detected.
Poster Session III

RISK MALIGNANCY INDEX IN THE EVALUATION OF THE ADNEXAL MASSES

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Evaluation of adnexal masses aid to choose who performs the surgery, and with the setting of the time schedule of the surgery. Risk of malignancy index (RMI), vaginal ultrasonography (US) and Ca125 serum marker are used to evaluate this. Methods: We studied retrospectively 158 patients treated in our hospital. We calculated statistical data. Results: Mean age was 45 years (15-88yrs). 60.2% were benign tumors, 10.1% low potential malignant tumors (LPMT), 17.1% primary malignant ovarian (Ov) and 2.5% metastatic tumors. We created four analysis groups: Ov, Ov+M1, Ov+LPMT and Ov+M1+LPMT.

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[Ultrasonography Data]

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[Ca125 Data]
### RMI Data

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**Conclusions:** RMI is the most useful tool.
Poster Session III

PREDICTORS OF RETAINED FOREIGN BODY AMONG PATIENTS UNDERGOING ABDOMINAL/ PELVIC SURGERY AND COSTS OF “ROUTINE” ABDOMINAL RADIOGRAPHS IN THEIR DETECTION

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Background: There is limited data on the use of abdominal radiographs in the intra-operative/post-operative period for detection of RFBs. As medical costs rise, hospitals have now planned to decrease reimbursement on conditions acquired during inpatient stays, including “unnecessary” radiologic studies.

Objective: To identify the clinical and demographic predictors of RFBs among patients undergoing major abdominal/pelvic surgery and associated costs of detection abdominal radiographs.

Materials and methods: Preliminary records of 125 patients who underwent selected abdominopelvic procedures from January 2002 to December 2010 at a tertiary-care academic hospital were reviewed. Cross-sectional prevalence study was conducted to identify predictors of RFBs.

Results: Median patient age was 47. Median weight was 80 kg. Median estimated blood loss(EBL) was 200cc. The most common procedures were an exploratory laparotomy (33.6%), open hemicolectomy (22.4%), reopening of recent laparotomy (18.4%) and total abdominal hysterectomy (16.8%). Thirty-one (24.8%) of cases were trauma. Four (3.9%) patients had a RFB. Three RFB cases were trauma laparotomies and one scheduled open hemicolectomy. Adjusted ORs were calculated for five possible risk factors: Age≥50 y vs. age< 50 y OR=1.70 (P=0.70), weight≥100 kg vs. weight< 100 kg OR=2.50 (P=0.73), EBL≥500cc vs. EBL< 500cc OR=0.82 (P=0.44), exploratory laparotomy (yes vs. no) OR=1.78 (P=0.61), trauma vs. non-trauma case OR=1.11 (P=0.93), and length of surgery (>3hours vs. < 3hours) OR=1.74 (0.66).

Conclusions: There were 4 RFBs, 75% were trauma cases. The other variables were not significantly associated with risk of RFBs. A policy on performing “routine” abdominal radiographs after a correct count in major surgery is unwarranted in certain cases.
Poster Session III

ULTRASOUND ACCURACY IN PREDICTION OF RECTOSIGMOID INVOLVEMENT IN ADVANCED OVARIAN CANCER PATIENTS

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Objectives: Residual disease after primary surgery is one of the most important prognostic factors in advanced ovarian cancer patients and the current standard of care is represented by the maximal surgical effort aimed at leaving no residual disease. Bowel resection is common intervention in experienced hands for achievement of optimal debulking. We analysed ability of transvaginal ultrasound to predict need of rectosigmoid resection.

Methods: Retrospective study comparing transvaginal ultrasound findings and histopathology and peroperative findings in advanced ovarian cancer patients (stages IIC-IV) surgically debulked at our department in years 2009-2011.

Results: In total, 214 patients were included into this study, in 88 of them, rectosigmoid resection was needed to achieve complete debulking and involvement of bowel serosa or wall was confirmed by histology. In 82 of them ultrasound predicted need of bowel resection. In addition, ultrasound indicated bowel involvement in 92 patients, however, in 10 of them the bowel was not affected (as assessed by surgeon). This gives the sensitivity for transvaginal ultrasound prediction of rectosigmoid resection 93.2% and specificity 92.1% (PPV 89.1% and NPV 95.1%).

Conclusion: Transvaginal ultrasound has high accuracy in prediction of rectosigmoid resection and thus allows for planning appropriate surgical team and conditions.

This work was supported by the Internal Grant Agency of the Ministry of Health, the Czech republic, project No. NT13070.
Poster Session III

HOME NURSING - HOME ADMINISTRATION OF ORAL CHEMOTHERAPY

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Background: Some patients receive home gyneco-oncologic oral chemotherapy, coordinated by an ambulatory oncology clinic, but without the benefit of nurses.

Common treatment failures:

1. Structured instructions from a nurse not administered.
2. No regular follow-up during treatment.
3. No records or reports of the treatment line.
4. No therapeutic continuum.

The literature states that a nurse as a treatment coordinator is a central resource to other staff members (Larson 1995).

We instituted oncologic nursing home-care coordinators in order to rectify said failures.

Goals:

· To provide comprehensive, continuous and structured nursing care.
· To develop the role of an oncological nurse coordinator for "Home oral chemotherapy".

Process and solutions:

· Staff and multi-disciplinary meetings.
· Formation of a role for a coordinating oncological nurse.
· Information brochures prepared for patients.

Intervention: Before treatment:

· Medical decision made to commence treatment.
· Patient interview
· Instruction of treatment protocol

Between cycles:

· Referral to blood tests in community
· Follow up in the gynecologic-oncology unit
· Telephone availability.

Summary and conclusions: Institution of an oncological nurse coordinator for this patient group led to the following benefits:
For patients:

- Improved treatment protocols
- Reduction in number of hospitalizations.

For caregivers:

- Improved level of professional care
- Improved monitoring and records - computerized records

A specialized nurse acting as a pivot for treatment administration is key for success in the efficient utilization of resources, and reduction of applications to ER. This intervention significantly improved patients’ level of knowledge and satisfaction.
Poster Session III

WOMEN'S PERCEPTIONS OF THE INFORMATION PROVIDED DURING TREATMENT FOR EARLY STAGE VULVAR CANCER

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1Gynaecological Cancer Centre, The Royal Hospital for Women, Randwick, 2School of Health, University of New England, Armidale, 3School of Women's and Children's Health, University of New South Wales, Randwick, 4School of Medicine, University of New England, Armidale, NSW, Australia

Background: There is paucity of information, particularly qualitative research, on women's experiences following treatment for early stage vulvar cancer. The aim of the present study was to describe women's experience of sexuality and body image following treatment for early stage vulvar cancer. Only one of four themes identified will be discussed in this paper.

Methods: A qualitative study design based on interpretive phenomenology was used to interview a purposive sample of 10 women who had previously being treated for an early stage vulvar cancer. Thematic analysis was used to derive themes that were essential to the experience.

Results: The mean age of the participants was 58 years. The theme 'information limitations', although not directly related to the study aim, was essential to the women's experience. Some women lacked access to basic information from diagnosis to consulting with a gynaecological oncologist, heightening fear and anxiety. Some described difficulty understanding the information they had been provided. Others had disregarded, or forgotten information that was not relevant to them at that point in time (sexual information). Many reported a lack of understanding of the extent of the surgical excision, or visualising what would be excised during their surgery, even some women unsure what the vulva actually incorporated. Some women felt unprepared for the discomfort they experienced.

Conclusions: The results of this study have identified information needs as a priority area to be addressed in future research. The findings also highlight areas that need improvement such as, access to timely and relevant information.
Maori women in New Zealand are twice as likely to develop cervical cancer when compared to Pakeha (European New Zealanders) and other non-Maori women. To compound this health disparity, they are almost three times as likely to die from cervical cancer. The New Zealand Cervical Screening Programme has sought to redress these alarming statistics and a number of culturally-specific initiatives have been introduced. These will be presented in addition to a project undertaken by the author, during postgraduate studies, that sought to increase cervical screening numbers in the Waikato region of New Zealand.
Poster Session III

QUALITY ASSURANCE OF SCREENING AND MANAGEMENT OF CERVICAL CANCER IN TAIWAN

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Taiwan National Cancer Registry was built in 1979 which collected 97% of diagnosed cancers countrywide.

To promote the quality of management for cervical cancer, National Health Research Institutes encourage the publication of guidelines based on current evidence and consensus. With the reference of National Comprehensive Cancer Network, Guidelines for Cervical Screening and Cervical Cancer had been published in 2004 and revised every 3 years. Indicators for quality assurance have been development since 2002 which include the proportions of patient with

(1) starting treatment within 6 weeks after the diagnosis of invasive cervical cancer;

(2) a complete pathological TNM staging if surgery is the initial treatment;

(3) histological negative resection margin if surgery is the initial;

(4) lymph node number ≥12 when surgery is the initial therapy for FIGO stage IA2 disease or above;

(5) starting radiation therapy within 42 days if radiation therapy is the initial;

(6) concurrent chemoradiotherapy as the initial treatment in FIGO IIB or above;

(7) adjuvant (chemo)radiation therapy within 120 days after hysterectomy of any type (negative indicator);

(8) completing radiation therapy within 63 days if radiation therapy is the initial and

(9) 5-yr overall survivals by FIGO stage.

The performance data for each institute are prepared by Civil Health Promotional Bureau, Department of Health annually.
[Proportion of starting treatment within 6 weeks]
[Proportion of LN number $\geq 12$ in FIGO IA2 or above]
[RT/CCRT after hysterectomy of any type]
SSH ..... LET’S TALK DIRTY! ADDRESSING THE EFFECTS OF TREATMENT FOR GYNAECOLOGICAL CANCER ON WOMEN’S SEX LIVES

E. Darragh¹, L. Holmes², I. White³, M. Instone⁴, K. Roberts⁵


It is estimated that 2 million people live with and beyond cancer in the UK and this figure will rise by 3% a year (NCSI 2011). More people are living with cancer as a chronic illness and adjusting to the consequences of treatment, often accepting of symptoms due to gratitude that they have “survived” the disease. Sexual difficulties following cancer treatments are readily recognised, as is the reluctance / ability of healthcare professionals to approach the subject.

No sex is not dirty! Demonstrating a willingness to talk about sexual concerns with patients may be the first step towards addressing women’s sexual recovery following cancer and its treatment. Legitimising discussions about sexual recovery within consultations could offer patients the opportunity to talk more about this often neglected element of patient management. Healthcare professionals should address their patient’s sexual rehabilitation needs and be aware of their level of competence.

The psychosexual subgroup identified the importance of healthcare professionals talking to patients about sexual health and has developed guidance on levels of intervention in addressing the sexual recovery of women with gynaecological cancer. The aim of this guidance is to provide a tool to support healthcare professionals in the management of women with disease and treatment-induced sexual difficulties.

The sub-group developed an educational tool based on the PLISSIT model with discreet levels of intervention dependent on experience, skill and knowledge. It addresses sexual function, concerns and difficulties that are relevant for women who have experienced any cancer, not just gynaecological.
Poster Session III

STANDARDIZED SCREENING FOR DISTRESS FOR WOMEN WITH GYNECOLOGICAL CANCER: A REVIEW OF TRENDS IN PATIENTS’ CONCERNS

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Background: Cancer and its treatments have more than a physical impact, with emotional, psychosocial, spiritual and practical consequences. Distress is a common response across the cancer journey for both patients and their families. Distress is conceptualized as an unpleasant experience of an emotional, psychological, social or spiritual nature that interferes with the ability to cope with cancer. Distress is a dynamic phenomenon, rising and falling over time, as events unfold. In particular it can be elevated for cancer patients at points of transition. These include such times as the initial diagnosis, start of treatment, end of treatment, at the point of recurrence and during the last days of living. Identifying and responding to distress is considered a critical aspect of quality care.

Methods: In a busy clinical setting, computerized tablets with the standardized Distress Thermometer, Edmonton Symptom Assessment System (ESAS) and Canadian Problem Checklist were used to capture data regarding a broad range of physical, psychosocial and practical concerns in order to better understand, respond to and provide patient-centered care.

Results: A review and analysis of data collected after one year of implementation of standardized screening identifies trends in patients’ concerns

Conclusion: This has allowed for identification of gaps in service and better resource allocation planning.
Poster Session III

CLINICAL OUTCOMES IN CO-ORDINATION BASED CARE FOR GYNAECOLOGIC ONCOLOGY PATIENTS BY SPECIALIST NURSES

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The state of Queensland, the second largest of seven Australian states (population 4.6 million) has one centralised Gynaecologic Oncology service, Queensland Centre for Gynaecologic Oncology (QCGC) located in the capital Brisbane.

There are three public treatment centres incorporated into QCGC which is located in the southeast corner of the state and all are within one hundred kilometre radius of each other. The majority of the state's population (3.1 million) resides in this area.

Access can therefore be a challenge due to the diverse nature of the state and distances involved to access many specialist services.

The Gynaecologic Oncology Nurses accept and triage referral from across the state and the neighbouring Northern New South Wales, adhering to the referral criteria developed by the unit directors, to ensure appropriate appointments are made and all investigations (where possible) are completed prior to initial consultation.

Communication with patients at diagnosis to ensure they understand information given to them and have the opportunity to ask any questions in relation to their consultation can generate confidence and hope to many women especially those in isolated regions of the state.

Access and Entry into a Multidisciplinary Centre where each case is discussed in a Multidisciplinary Team Meeting (MDTM) to ensure best clinical practice and appropriate outcomes are achieved both pre and post treatment and through ongoing clinical follow up.
Poster Session III

ROLE OF ADVANCED PRACTICED NURSE IN GYNAECOLOGY ONCOLOGY IN SINGAPORE

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Advanced Practice Nurse (APN) is a Master prepared Registered Nurse who have met advanced educational and clinical practice requirements beyond the basic nursing education required of RNs for extended practice. She assumes a clinical role and uses research to improve patient outcome. The APN works collaboratively with the doctor to manage and treat patient's condition utilizing skills like assessing, planning, evaluating and initiating treatment needs of the patients. We provide holistic and compassionate care for Gynae-oncology patient in collaboration with multi-disciplinary team members. Our clinical management involves history taking, physical examination, order and interpret laboratory results as well as initiating treatment within the framework of our advanced nursing practice.

We perform ward rounds and clinic sessions with our clinical supervisors; provide pre-treatment counselling, managing post treatment complication and follow-up of well recovered patients. We also perform procedures like bedside abdominal paracentesis, wound debridement, secondary suture, pap smear, injecting thrombolytic agent for occluded central line. In addition to this clinical management, we also initiate education for individual, families on their health condition, treatment plan, and complication prevention. We also aim to provide clinical leadership and consultancy in establishing and monitoring standards of practice to nursing staff. This presentation will provide an overview of how this role has enhanced the experience of patients journey through cancer and cancer treatment.
Poster Session III

HOLISTIC MANAGEMENT OF GYNAE-ONCOLOGY PATIENT: CASE SCENARIO

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Diagnosis of cancer very often affects the individual and their love ones physically, psychological and socially. Nature of disease also requires involvement of multidisciplinary team members. In Gynaecology Oncology, we aim to provide holistic and compassionate care by collaborating with multi-disciplinary team members and to strive towards a centre of excellence in providing the highest quality services to women with gynaecological cancer and their families.

We present a case scenario of a patient, Mdm CML, who was diagnosed with ovarian cancer and had recurrence disease with complication of intestinal obstruction, enterocutanous fistula, and sepsis shortly after she had completed her treatment. There was a lot of frustration, disappointment and loss of faith as her disease progressed and it had affected the family as a unit.

As an APN working in the unit, we are able to collaborate with the doctors to manage and treat patient’s condition utilizing skills like assessing, diagnosing, planning, evaluating and initiating treatment needs of the patients. With better understanding of the disease process, in addition to the rapport built with patient and family, we are able to provide the necessary treatment, care, counselling and support to them.

Collaborative management between the doctors, allied health professionals and the APN will be illustrated.
Poster Session III

ROLE OF THE ONCOLOGY NURSE IN A SEXUAL HEALTH CLINIC FOR GYNECOLOGIC CANCER SURVIVORS

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Gynecologic cancer treatment has physical and psychosocial consequences that influence changes in quality of life. In particular, treatment can impact sexual function and sexuality.

Our cancer centre has created a specialized clinic to address sexual health and quality of life following treatment. The nursing role in this clinic is a key component to the success of this interprofessional service.

The nurse is a specialized oncology nursing role with focused preparation in sexual health issues. The initial clinic visit involves an in-depth assessment by the nurse using a customized tool designed for this purpose together with other standardized measures. The customized assessment tool is based on the Supportive Care Framework and helps to prepare for tailored intervention related to physical, psychosocial, informational and practical patient concerns. Brief counseling and education are provided by the nurse and individualized resource packages are provided. The patient returns for a second appointment with the physician and nurse together.

Patient feedback has been very positive with rating on satisfaction with the clinic being primarily “very satisfied”. In particular, women reported their information needs have been met. Learning how to better manage the effects they were experiencing and learning more about community based resources were cited as helpful. Satisfaction with the nursing role was also evident.

This presentation will describe the nurse’s role and preparation in the sexual health clinic for gynecologic cancer survivors. The nature of the practice will be described in terms of types of issues the nurse manages and resulting impact on patient outcomes.
Poster Session III

A REVIEW OF GYNECOLOGIC ONCOLOGY CASES PERFORMED WITHIN A 5-YEAR PERIOD IN A TERTIARY REFERRAL HOSPITAL IN ANKARA, TURKEY

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Aims: To review final results of gynecologic oncology cases performed in Zekai Tahir Burak Women's Health and Research Hospital in Ankara, Turkey.

Methods: Hospital cancer registry database was reviewed for gynecologic oncology cases performed between January 2007 and January 2012.

Results: A total of 1277 malignant cases were identified during a five-year period. Endometrial cancer including sarcoma was diagnosed in 489 (38.3%) cases, cervical cancer in 338 (26.4%) cases, ovarian cancer in 320 (25%) cases, vulvar cancer in 30 (2.3%) cases, tubal cancer in 18 (1.4%) cases, primary peritoneal carcinoma in 30(2.3%) cases, vaginal cancer in 8 cases(0.6%), gestational choriocarcinoma in 6 cases(0.4%), gastrointestinal cancer in 28 cases(2.1%), urinary bladder cancer in 2 cases(0.1%), lymphoma in 3 cases(0.2%) and malignancy of unknown primary in 5 cases(0.4%).

Conclusions: In tertiary referral centers, various gynecologic oncological as well as non-gynecologic malignancies are encountered. Multidisciplinary approach is crucial especially in cases with non-gynecologic tumors.
HEALTH BELIEF MODEL SCALE FOR CERVICAL CANCER AND PAP SMEAR TEST: PSYCHOMETRIC TESTING

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Background: While the Champion Health Belief Model scales have been tested extensively for breast cancer and screening for it, the evaluation of Health Belief Model scales in explaining the beliefs of women with regard to cervical cancer and the Pap smear test has only received limited attention.

Aim: The aim of the study was to develop and test the psychometric properties of the Health Belief Model Scale for cervical cancer and Pap smear testing.

Methods: This methodological research was carried out in a city in Turkey between August and October 2007. The data were collected from 237 randomly selected women who met the criteria for inclusion and agreed to participate in this study. The Champion Health Belief Model scales were translated into Turkish, adapted for cervical cancer, validated by professional experts, translated back into English and pilot tested.

Results: Factor analysis yielded five factors: Pap smear benefits and health motivation, Pap smear barriers, seriousness, susceptibility, and health motivation. Cronbach alpha reliability coefficients for the five subscales ranged between 0.62 and 0.86, and test-retest reliability coefficients ranged from 0.79 to 0.87 for the subscales.

Conclusion: The Health Belief Model Scale for Cervical Cancer and the Pap Smear test was found to be a valid and reliable tool in assessing the women's health beliefs. Understanding the beliefs of women in respect of cervical cancer and Pap Smear test will help healthcare professionals to develop more effective cervical cancer screening programmes.
Poster Session III

NURSING AND HEALTH CARE

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Background: The incidence of health care problems e.g. heart problems in Lahore, Pakistan is 55.7 per 100,000 with serious presentation in last stages being common (≥ 50%). The most pragmatic solution to early control lies in health care education. Nurses constitute a special group having characteristics most suited for delivering health care information to the patients. We assessed the level of knowledge among nurses in teaching hospitals of Lahore. We also identified whether selected factors among nurses were associated with their knowledge of health care risk factors, so that relevant measures to improve knowledge of nurses could be taken.

Methods: A cross-sectional survey was conducted in many teaching hospitals using stratified random sampling with proportional allocation. Knowledge of health care risk factors was categorized into good, fair and poor categories.

Results: Forty percent of nurses had good knowledge of risk factors. Graduates from nursing schools (aOR = 4.52, 95% CI: 2.93, 6.10), nurses who had cared for patients (aOR = 2.42, 95% CI: 1.00, 1.99), those having received a health care training themselves (aOR = 2.1, 95% CI: 1.08, 2.26) were more likely to have good knowledge.

Conclusion: A relatively small proportion of the nursing population had good level of knowledge of health care risk factors. This knowledge is associated with nursing education and training and nursing school status. Since only about one-third of the nurses had good knowledge about risk factors, there is a need to introduce health care education at one step above to the present level in nursing institutes.
Poster Session III

RELATIONSHIPS BETWEEN STIGMA RELATED TO HUMAN PAPILLOMAVIRUS, SEXUALLY TRANSMITTED INFECTION AND INTENTION TO GET HPV TEST IN KOREAN WOMEN

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Objective: This study was performed to identify the stigmas related HPV and STI, the intention to get HPV test and to examine their relationships.

Methods: Survey was done in Korean women visiting gynaecology department of hospital. Stigmas related HPV and STI were assessed using 7 items on a 4-point scale and intention to get HPV test was assessed using 1 item on a 5-point scale. Differences and correlations between stigmas related STI and HPV were analysed using Wilcoxon signed rank test and Spearman Rho coefficients.

Results: Participants included 462 women. HPV stigma were lower than STI stigma (z =5.47, p< .001), but their correlations were high (Rho=.693, p< .001). Women who knew HPV as a STI was higher in HPV stigma than did not (χ² = 25.32, p< .001). There was not different in HPV stigma between women had HPV test and women had not (z= -0.07, p=.948). HPV stigma was correlated with intention to get HPV test (Rho=.34, p< .001). Only 4.5% of women had a chance to get HPV test and 68.4% of women had intention to receive HPV test.

Conclusions: HPV awareness as a STI was associated with perception of HPV stigma. HPV education should be given especially for women to get HPV test and de-stigmatizing HPV as a STI is necessary for Korean women.

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Poster Session III

WOMEN’S EXPERIENCES AFTER A RADICAL VAGINAL TRACHELECTOMY FOR EARLY STAGE CERVICAL CANCER

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A radical trachelectomy is a fertility sparing operation which involves removal of the cervix and placement of an isthmic cerclage. This descriptive phenomenological study explores women’s long-term experiences.

Method: Twelve women from two UK cancer centres were selected using purposive maximal variation sampling, including women 1-10 years since surgery with varied fertility outcomes and additional related procedures. Semi-structured, in-depth telephone interviews explored quality of life, sexual health and support needs.

Findings: Initial reactions were similar to other cancer survivors including a sense of ‘no other option’ and feeling ‘lucky’. Several had a positive experience; increased closeness to family and a changed outlook on life. Meanings were closely related to childbearing ability. A few experienced delayed negative psychological reactions and worries about recurrence. Isolation and the wish to contact similar others were recounted by many. Single women appeared to have additional body image challenges. Pregnancy created anxiety for some and a miscarriage or complex birth was intensely emotional. Persistent side effects for some included mild lymphoedema, paresthesia, changes in menstrual or sexual function. Altered menstruation appeared to be the most bothersome. Sexual function was not a long term concern for most, but some noticed changes for which they had developed self-adaptive strategies.

The Gynaecological Clinical Nurse Specialist, family/friends, online forums, treating consultant and a trachelectomy support group were supportive. Unmet needs were related to statistics; pregnancy recommendations; counselling; isolation and increased public/professional awareness. This study helps to inform clinical practice by identifying areas of unmet need and areas needing further exploration.
Poster Session III

TEACHING GYNECOLOGICAL MALIGNANCY CARE TO MEDICAL STUDENTS; CAN A VIRTUAL LEARNING ENVIRONMENT HELP?

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In 2006 Moodle, a freeware virtual learning environment package, was introduced to the Department of Obstetrics & Gynecology at RCSI. In excess of 1500 students have since passed through the course to date. The Department of Obstetrics and Gynecology were one of the first adopters of this technology. Each year we have developed the course following an analysis of student on line activity and correlations between Moodle based assessments and end of year exam results.

We explain how Moodle facilitates flexible consistent teaching over five student groups over five different hospital locations.

As none of our teaching hospital sites are cancer centers, direct student access to gynecological oncology is minimal. We successfully deliver the gynecological oncology course virtually through Moodle. We demonstrate how our multimedia supported blended learning provides a foundation for our medical students.

We demonstrate how we maintain consistency in delivering our program across hospital sites, and meet the aims and objectives of the curriculum.

We also discuss the findings of our annual web based questionnaire in the context of innovation within the Obstetrics & Gynaecology course delivery, assessment and development. We outline the features which have allowed the course be so highly regarded by students.

Moodle is now fundamentally embedded into the department’s delivery of the Obstetrics and Gynecology curriculum, and an absolute necessity in the consistent delivery of our gynecological oncology course.
Poster Session III

COMPARATIVE STUDY ON MARITAL INTIMACY OF GYNECOLOGIC CANCER PATIENTS AND GENERAL WOMEN

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Background and aims: Cancer and its treatment can have a significant effect on the intimacy of both people with cancer and their partner. This study is to evaluate the marital intimacy by comparing intimacy between gynecologic cancer patients and general women.

Methods: A total of 15 patients treated for gynecologic cancer and a total of 15 general women were recruited between March and April 2012. Each subject was assessed for marital intimacy by Marital Intimacy Scale, and semi-structured interview. Marital Intimacy Scale composed of 3 items in 15 questionnaires - Cognitive, Emotional, Sexual intimacy. The data analyzed by percent, mean, standard deviation, Mann-Whitney U test using SPSS 18.0 program.

Results: The patient population has mean age 43.73(±5.5) years. Subjects were diagnosed with cervical cancer (33.3%), ovarian cancer (66.7%). Marital intimacy (the total score) for patients with gynecologic cancer was 48.6(±7.99, range, 27-59). Cognitive intimacy score was 18.8(±1.93, range, 15-24). Emotional score was 16.5(±3.74, range, 6-21). Sexual intimacy score was 13.3(±4.35, range, 6-19). The general population has mean age 44.2(±3.0) years. Marital intimacy (the total score) for general population was 61.4(±8.37, range, 52-75). Cognitive intimacy score was 20.9(±2.37, range, 18-25). Emotional score was 21.2(±3.43, range, 15-25). Sexual intimacy score was 19.3(±3.31, range, 15-25). Marital intimacy (total score, cognitive, emotional, sexual score) of gynecologic cancer patients was significantly lower than general women (p=.001, p=.015, p=.001, p=.001).

Conclusions: Marital intimacy is central aspect of quality of life. Therefore, to improve patients' quality of life, healthcare professionals have to recognize and support.
Poster Session III

THE USE OF HEALTH COMMUNICATION FOR COMMUNITY PARTICIPATION IN PROMOTION OF VOLUNTARY BLOOD DONATION IN NIGERIA

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Health communication is aimed at ensuring behavioural change among the populace regarding practices that promote optimal health. This activity may be formal or non-formal in setting which encourages community participation for health promotion. However, evidence-based studies in Nigeria involving use of health communication have been limited to infotainments with limited attention paid to community participation in voluntary blood donation. This study therefore, determined the use of health communication for community participation in promotion of voluntary blood donation in Nigeria.

The study adopted qualitative method of data collection. A total of 440 participants from four LGAs in Owerri senatorial zone of Nigeria were interviewed. A validated FGD guide was formulated and tested for the study. Four Focus Group Discussions (FGDs) were carried out in each of the four LGAs in the senatorial zone totalling sixteen in number. The FGDs were analysed thematically using content analysis.

The results revealed that majority of the FGD participants were unanimous in their opinion that community participation in voluntary blood donation was non-existent due to community members' knowledge, attitude and awareness about voluntary blood donation. However, significant behavior change in this regard would be achieved through adequate health information and communication. Most participants in the female and male's sessions were of the view that community communication strategies should be tailored to promote their participation in voluntary blood donation.

Therefore African governments should support establishment of community-based communication strategies to promote community-participation in promotion of voluntary blood donation in order to save lives of most African-people.
Poster Session III

THE GYNECOLOGIC LITERATURE: BEAST OF BURDEN OR MONSTER?

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Background: 58 journals reporting findings relevant to gynecologic oncology (2010-2012) were examined. They were assessed for relative impact and cost.

Methods: The journals considered were evaluated in terms of current impact factor (IF), change in IF, eigenfactors (EF), and article influence scores (AI). Subscription costs were obtained from publisher information.

Results: CA-Cancer J Clin had the highest IF (94.3) & AI (100) and second highest EF (99). Nature Review Cancer, the Journal of Clinical Oncology & Lancet Oncology were cancer specific journals with IFs>15, while the top EF journals were The Journal of Clinical Oncology, Cancer Research & Clinical Cancer Research. Rankings for The International Journal of Gynecologic Cancer and Gynecologic Oncology were: IF = 56/58, EF = NA, AI = NA (IJGC) & IF = 45/58, EF = 33/58 , AI = 49/58 (GO). The current IF improved from the 5 year IF in 31 journals (including GO, 16/31) and decreased in 18 (including IJGC, 13/18). Subscription costs were $60-1350 (members), $162-4600 (non-members) & $60 for CA otherwise $650-7610 (institutions/library).

Conclusions: The extreme utilization of review information in Nature Review Cancer and CA illustrated by the IF indicates a role as a beast of burden in the literature, probably as the leading source of quoted cancer statistics (CA). Rankings for IJGC & GO likely reflect the small size of the specialty. The decreased IF in 37% of the journals may reflect the international economy's effect on cancer research. Subscription costs have monster proportions and appear unbearably high for individuals and institutions alike.
Poster Session III

TEN TOP TIPS FOR CANCER SURVIVORSHIP: A PROMPT FOR CANCER PATIENTS AT THE END OF THEIR PRIMARY TREATMENT.

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Background: In the UK 2 million people are living beyond cancer treatment and they frequently have unmet needs at the end of treatment (Macmillan, 2010). Current evidence points towards health services needing to be provided in the period after cancer treatment but at present such support is not always well coordinated and may come from a variety of sources.

Methods: The CCaT (Consequences of Cancer Treatment Collaborative www.cancerconsequences.org) group are 12 clinical academics working in the field of cancer survivorship, brought together as part of the UK National Cancer Survivorship Initiative. The Top Tips were designed to empower cancer survivors and ensure that they could access the care and support they need for future wellbeing. The leaflet was compiled in partnership with cancer survivors, GPs and oncology health care professionals.

Results: The leaflet was developed with 10 key headlines and a short description to help guide patients as to what care they should expect to receive. These were:

1. End of treatment assessment
2. Plan of care
3. Who to contact
4. Managing symptoms
5. Worries about cancer
6. Healthy living
7. On-going check-ups
8. Day to day concerns
9. Talking about your feelings
10. Make suggestions and get involved.

Conclusions: These evidence based ten top tips have been designed to help orientate cancer survivors as to what to expect once they have finished their treatment and self-manage their survivorship into the future. This could have long term benefits for their health, their well-being, and for the wider health economy.
Poster Session III

MINDFULNESS-BASED COGNITIVE THERAPY FOLLOWING GYNAECOLOGICAL CANCER TREATMENT: A FEASIBILITY STUDY

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Background: Fear of recurrence is a significant cause of distress to women following gynaecological cancer. Some women develop depression and anxiety disorders as a result that can severely disrupt relationships and quality of life. Mindfulness-based cognitive therapy (MBCT) is well-established within UK national guidelines as a treatment for the prevention of recurrent depression.

Our aim was to develop protocols for an MBCT intervention for cancer survivors and undertake four 'test' programs. A realistic evaluation of intervention acceptability, validated measurement tools, recruitment rate and attrition of patients was also undertaken.

Methods: A systematic review of the literature and a focus group with patients and a gynaecological oncology team resulted in the development of 8 weekly 2 hour sessions. Twenty four women (mean age 58 years, range 26 - 70) survivors self-selected to take part as an MBCT learning community. Qualitative interviews were undertaken with participants (n=18) and a focus group at the end of each programme (n=4).

Results: An MBCT - cancer programme was developed which interview data confirmed to be acceptable to women. Recruitment was found to be difficult initially, but the time from end of treatment (at least 6 months) was found to be crucial to successful engagement. Qualitative evaluation data described unanticipated benefits of improved sleep and reduced feelings of isolation.

Conclusions: MBCT can potentially be an appropriate intervention to support resilience and reduce distress in women who are struggling with fear of recurrence. A pilot trial would be recommended from this feasibility work.
Poster Session III

THE LIVED EXPERIENCES OF WOMEN UNDERGOING OVARIAN CANCER SURGERY

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Background: Ovarian cancer is the leading cause of death among Western World women suffering from gynecological malignancies. The treatment is long, complex and aggressive, as it consists in extensive primary surgery followed by chemotherapy.

Aim: Aiming to provide a patient perspective on being newly diagnosed and starting treatment for ovarian cancer, personal experiences were explored during diagnostics and commencement of treatment.

Method: Women, who underwent surgery for various stages of ovarian cancer, participated in qualitative research interviews the day before and eight weeks after their surgery. The interviews followed a semi-structured guide. By applying a phenomenological-hermeneutic text interpretation methodology, the findings were systematically identified, put into meaning-structures, and analysed.

Results: The diagnosis and start of treatment represented an extensive life event, where personal existence was threatened, yet vitality and hope for a cure were present. A high level of trust in healthcare was found, and the necessity of the operation was not questioned. The women considered the surgical procedure to be dangerous, and a need to reflect on their personal death generated. Creating disease-free zones and maintaining everyday-life represented significant coping strategies. Positive family relations represented a resource, whereas less supportive relations represented a barrier in going through with treatment. Basic care induced and strengthened hope and vitality.

Conclusions: The individual ability to go through with treatment seemed deeply influenced by personal lifestyle, social conditions, coping strategies and experiences of hope. By offering targeted family counselling and caring for general health and wellbeing, hope can be sustained and early rehabilitation initiated.
Poster Session III

OVARIAN CANCER SURGERY: HEALTH AND COPING DURING THE PERIOPERATIVE PERIOD

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Background: Ovarian cancer surgery is predominantly elective. This circumstance allows for intervening during the wait for surgery, in terms of preparing the patients for the forthcoming treatment.

Aim: To survey general health and coping in women undergoing ovarian cancer surgery, and to develop and test a supportive care intervention.

Methods: Women, who underwent surgery on the suspicion of ovarian cancer participated in a follow-up questionnaire study, in which the Short Form-36 and the Life Orientation (SOC) questionnaires were used to survey health and coping during the perioperative period. Subsequently an evidence-based, preoperative supportive care programme was developed and tested.

Results: From 294 women allocated to three study groups, 546 Short Form-36 and 253 SOC questionnaires were available for analysis. The response rate was 86%. During the perioperative period the women reported deterioration in physical health; however, the majority stayed within standard levels. In contrast to this, the mental health status was, although increasing, below standard levels during the full study period. This also applied to women who had their cancer diagnosis refuted. The coping capacity was close to normal levels.

Conclusions: A need for supportive care during the perioperative period was identified. This should be adjusted to the nature of the disease and the extent of the treatment. Participation in a supportive programme can support the physical health during the perioperative period; however, a further addressing psychosocial aspect seems required.
Poster Session III

A SURVEY ASSESSMENT OF GYNECOLOGIC ONCOLOGY TRAINING AND SERVICES IN LATIN AMERICA AND THE CARIBBEAN

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Introduction: Collective knowledge is lacking about the landscape of gynecologic oncology (gyn-onc) training and service provision in Latin America and the Caribbean (LAC).

Objective: To conduct a survey assessment of gyn-onc training and services in the LAC region from the perspective of healthcare providers.

Methods: A survey was emailed to IGCS, SGO, and ACOG members from LAC. Additional emails were obtained through internet research. Online survey software was used to analyze data with descriptive statistics.

Results: 244 surveys were sent; 124 (50.8%) responded, representing 24/30 countries in LAC. Most respondents were gyn-onc (61.2%) and work in a public hospital affiliated with a university/medical school (58.9%). 45.8% stated that there is no formal certification board for gyn-onc in their country. Of those gyn-oncs who work in a country where there is formal certification, 20.3% are not board-certified. Regarding type of gyn-onc training, 73.0% completed a formal fellowship in gyn-onc, 24.3% an apprenticeship with a gyn-onc, and 2.7% general surgery/surgical oncology. Of the 24 represented countries, 8 (30%) have no gyn-onc training. At their respective institutions, 58.2% stated that gyn-oncs never administer chemotherapy, 25.2% said that surgeons other than gyn-onc operate on gyn-onc patients very frequently/always, 36.4% have no palliative care specialists, and 51.8% have no hospice care.

Conclusions: Many countries in the LAC region lack the ability to provide comprehensive gyn-onc training and services. The development and standardization of gyn-onc training and services in the LAC region should be emphasized.

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Poster Session III

A SURVEY ON HUMAN PAPILLOMAVIRUS AWARENESS AND ACCEPTANCE OF VACCINATION AMONG NURSING STAFF AND TRAINEES IN ANKARA, TURKEY

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Aims: To assess the awareness about human papillomavirus (HPV) infection, its link with cervical cancer and acceptance of prophylactic vaccination among nurses and nurse trainees in the capital city of Turkey.

Methods: Between August 2011 and February 2012, staff nurses and nurse trainees completed a 17 item questionnaire. Data on education level, sociodemographic factors, knowledge of HPV virus, routes of spread, HPV related diseases, vaccination, also participants’ willingness for vaccination were collected.

Results: Among 350 participants, 87.7% had previously heard of HPV virus. Thirty-nine percent were informed by media organs such as radio and television. Only 14% were informed by a healthcare provider. In 46% of the study population, information was acquired from non-professional sources such as friends and family members. Twenty six percent knew the ways of contamination, 81.7% was aware of the link between HPV and cervical cancer, 80% had heard of prophylactic vaccination, 67.1% were willing to be vaccinated, 74.9% had intent to vaccinate their daughters, 71.1% had intent to vaccinate their boys, and 80.5% had knowledge about the recommended age of vaccination.

Conclusions: This study demonstrated that there was an important lack of knowledge about HPV, HPV related disease prevention and prophylactic vaccination among nurse trainees, who are candidate healthcare providers. These results reflect the need of public awareness and educational programs about HPV and prevention methods, especially in the subgroup of younger women, in order to diminish the prevalence and negative consequences of this infection.
Poster Session III

THE DISPARITY IN GYNECOLOGIC CANCER RESEARCH BETWEEN THE RICH AND THE POOR

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Introduction: Seventy percent of all deaths due to gynecologic malignancies occur in low and lower middle income countries. Most often comprehensive cancer care is not available or insufficient. Research aimed at identifying appropriate prevention and treatment benefiting those most in need is much needed.

Objective: To identify the proportion of gynecologic cancer research originating in low and lower middle income countries.

Method: A search strategy was developed that identified all papers with a gynecologic oncology topic published in 2010 and indexed in Pubmed. In this cohort all papers published in a low or low middle income country as defined by the World bank or from a resource poor country were selected and further analysed.

Results: In 2010 1437 papers were published and indexed in Pubmed with gynecologic oncology as topic. Only 35 (2.4%) were originating in a low or lower middle income country or had cancer treatment or prevention in a low resource setting as topic.

Corresponding authors from Turkey, Thailand and Korea together published 21/35 papers. Two papers came from Africa, none from South America. While 66 papers reported on clinical trials none of these trials were reported on by authors from poor countries.

Conclusion: There is a severe disparity worldwide between the poor countries that carry the burden of gynecological cancers and the rich countries in which all research is done. There is a great need for building research capacity in low resource countries and participation of low resource cancer centers in multi center trials.
Poster Session III

CLINICAL TRIALS UNDERREPRESENTATION OF PATIENTS OVER 70 YEARS WITH GYNECOLOGICAL CANCER: AN UNSOLVED DISCUSSION

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Aims: Ovarian, endometrial, cervical and vulvar cancers are often found in elderly women. There is a lack of clinical trial data about gynecological cancer in advanced age. Aim of this paper is to describe tolerance and toxicity to chemotherapy in elderly patients with gynecological cancers.

Methods: Retrospective analysis. We selected patients over 70 years with gynecological cancer treated in our Institute between 2005 and 2012. Data about diseases, treatments and toxicities were collected.

Results: Seventy six patients over 70 years, of these 19 over 80, treated for ovarian, endometrial, cervical or vulvar cancer. Ovarian cancer was the most frequent (58%), followed by endometrial (17%), cervical (14.5%), vaginal (4%), vulvar cancer (2.5%) and uterine sarcoma (4%). The 69% of patients were treated with polichemotherapy. The 62% underwent to a single line of treatment, 38% to several lines. Nine patients were recruited in clinical trial. Sixty nine patients (90%) completed treatments without major complications, 7 patients interrupted therapies for toxicity. Hospitalization has been necessary in 5 patients (6.5%). Hematologic toxicity was the most frequent (47%), requiring blood transfusion in 6 patients (7.9%), hematopoietic growth factors in 4 patients (5%). Dose reduction has been necessary in 10% of cases.

Conclusions: Patients over 70 years with gynecological cancer are underrepresented in clinical trials. Our results show a low profile of toxicity despite polichemotherapy.

It is important to offer to the elderly patients with gynecological cancers the standard treatment, including the recruitment in clinical trials.
Poster Session III

FOLLOW-UP OF GYNECOLOGICAL CANCER PATIENTS AFTER TREATMENT - THE VIEWS OF EUROPEAN EXPERTS IN GYNECOLOGIC ONCOLOGY

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Objective: Follow-up after treatment for gynecological cancer demands large resources. Still, evidence of efficacy is lacking. The aims of this survey were to explore follow-up routines among European experts in gynecological oncology, and to ask for their views regarding standard of care for such practice.

Methods: An anonymous survey was e-mailed to all members of the European Society of Gynecological Oncology and the Nordic Society of Gynecologic Oncology. Main outcome measures were surveillance routines and the clinical experts' evaluation of evidence and view of follow-up in hospitals versus at general practitioners (GPs).

Results: The number of visits recommended by a majority of the responders was in line with current guidelines. The use of surveillance tests varied considerably. Vaginal vault cytology was routinely used in follow-up of 56% of the cervical cancer patients and 37% of the endometrial cancer patients. 57% of the experts considered less intensive follow-up for low-risk patients as adequate. Significantly more responders from low-economy countries preferred conventional hospital follow-up for all patients compared to responders from high-economy countries (p < 0.001). Responders stating that they were aware of the low evidence level of the follow-up routines were more willing to consider follow-up by GPs.

Conclusions: Follow-up routines vary in Europe. According to the responders of this survey, follow-up by GPs may be an option for low-risk patients. New follow-up routines of gynecological cancer should be based on prospective trials comparing conventional follow-up with alternative methods of care, assessing survival, detection of recurrence, and quality of life.
Poster Session III

LOW MNA SCORE AND THROMBOCYTOPENIA ARE PREDICTIVE OF UNEXPECTED HOSPITAL ADMISSION DURING TREATMENT IN ELDERLY PATIENTS RECEIVING CHEMOTHERAPY


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Background: Treating older cancer patients can be a challenge to oncologists and demands integration of several variables to tailor individualized therapy avoiding excessive toxicity. Clinical, biological, and molecular predictors of chemotherapy-related toxicity have been identified but not necessarily validated.

Methods: From 2002 to 2005, we collected data of 364 older cancer patients (≥70 years) from 11 centers in south-west France enrolled in a prospective trial. Every patient was proposed a comprehensive geriatric assessment (CGA). Medical oncologists prescribed treatment blinded from CGA result according to their standard practice and three treatment groups where prospectively defined before treatment initiation: standard, reduced, and adapted/symptomatic.

Hospitalization for treatment toxicity served as an indicator for severe toxicity. Clinical and biological variables known or suspected to be associated with toxicity were first analyzed in a univariate model. Variables significant at the 5% level in the univariate analysis were considered for the full multivariate logistic regression model.

Results: Overall, 165 patients (45.3%) received standard treatment, 53 patients (14.6%) had reduced treatment, and 146 patients (40.1%) had adapted (palliative) treatment according to the investigator's decision. After multivariate analysis, only thrombocytopenia (OR 3.76; 95%CI: 1.3 to 10.8) and low Mini Nutritional Assessment (MNA) score (OR 4.19; 95%CI: 1.7 to 10.3) were associated with higher hospitalization rate, hence severe toxicity. Adaptive chemotherapy schedule and/or doses reduced significantly the risk of hospital admission (OR 0.51; 95%CI: 0.26 to 0.99).

Conclusions: We suggest that Mini Nutritional Assessment should be part of the baseline geriatric evaluation accomplished by oncologists before initiating anticancer treatment.
Poster Session III

VASCULOGENIC MIMICRY WITH MMP-9, LAMININ AND VE-CADHERIN EXPRESSION IN MALIGNANT OVARIAN TUMORS

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Background: Vasculogenic mimicry (VM) is an alternative tumor vascularization pathway related to matrix metalloproteinases (MMP's) activation via their cleavage of laminin and VE-cadherin which promotes the adherence of the VM channel wall to tumor cells.

Objective: To explore the existence of vasculogenic mimicry in ovarian tumors and its correlation with the clinicopathologic features.

Methods: 74 women with ovarian tumors (52 primary invasive cancers, 9 borderline tumors, 7 metastatic and 6 benign tumors) were collected with complete clinical data. CD34 immunohistochemistry for microvessel density (MVD) and PAS stain were used to investigate VM in the tumor tissue. Immunohistochemical staining of VE-cadherin, laminin and MMP-9 were used to explore their possible relationship with VM formation.

Results: A total of 33 (44.6%) invasive cancers expressed evidence of VM. Tumor clinical stage (p=0.01), pathologic grades (p=0.01) and histological types (p=0.001) were significantly different between the VM and non-VM groups. Median MVD in malignant masses was 25 per HPF (range:16-38) and VM was more frequently found in tumors with low MVD (MVD< 24/HPF; p=0.02). Expression of laminin (p=0.000037) was significantly higher in the VM group than in the non-VM group. The differences in VE-cadherin expression in VM positive tumors vs. other tumors were close to statistical significance (p=0.051). MMP-9 expression was not significantly different (p=0.09).

Conclusions: Vasculogenic mimicry exists in ovarian cancer and a high grade malignancy is accompanied by a high incidence of VM formation. Elevated expression of laminin and VE-cadherin may contribute to the formation of VM in malignant ovarian tumors.
PERIOPERATIVE USE OF INFERIOR VENA CAVA FILTERS IN NORTHERN IRELAND REGIONAL GYNAECOLOGY CANCER CENTRE OVER A 5 YEAR PERIOD

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Background: Information on peri-operative use of IVC filters in gynaecology is sparse. Filters probably protect from PE in the peri-operative period, but increase subsequent incidence of DVT, and have not been shown to increase overall survival. The FDA recommend removal as soon as protection from PE is no longer required.

Aims: To describe experience with IVC filters over a 5 year period. To assess impact of implementation of an IVC filter guideline.

Methods: Retrospective case review 2007-2012.

Results: 24 women with preoperative IVC filter and major thrombo-embolic disease (19 proximal DVT ± PE, 5 proven PE with pelvic mass). 19 malignancies (16 ovarian, 3 non-ovarian), 2 borderline tumours, 3 benign pelvic masses. After guideline implementation, we standardised anti-coagulation practice. The mean number of pre-op filter days fell from 8.6 to 3.9, and post-operatively from 19.7 to 10.2 days. We increased the proportion of cases who had retrieval attempted. Early complication rate was 13%, and the late complication rate was 31% in people with retained filters.

Conclusions: IVC filters should be reserved for high risk cases with a strong indication for insertion. Retrievable filters should be used when appropriate. Long term filter retention is inevitable in significant proportion of cases (39% of our cases). A guideline can help co-ordinate care between gynaecologists, haematologists and radiologists and will help reduce filter duration, and ensure adequate anti-coagulation throughout. It is not possible to state conclusively whether filters were of net benefit as numbers were small and there is no comparison group.
Poster Session III

ADENOCARCINOMA OF THE SPLEEN AND PANCREAS METASTATIC FROM THE FALLOPIAN TUBE AS PART OF A LIVE LIVER DONOR EVALUATION

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Background: This is a case of a 48 year old woman who originally presented to the transplant department as a potential live liver donor for her brother-in-law who suffers from hepatitis C complicated by partial portal vein thrombosis, ascites, spontaneous bacterial peritonitis, and encephalopathy. As part of the preoperative workup, the patient received a CT scan which showed an incidental 4cm mass in the tail of the pancreas. She was ruled out as a potential liver donor based upon the finding of this mass.

Methods: She underwent a distal pancreatectomy and splenectomy with a final pathology consistent with a high grade adenocarcinoma with papillary features and psammomatous calcifications, possibly originating from a gynecologic malignancy. The tumor cells were positive for CK7, P53, and WT-1; CA125 was markedly elevated - all of which are commonly associated with gynecologic cancers. The patient had no gynecologic symptomatology. She underwent a total abdominal hysterectomy, bilateral salpingoophorectomy and staging in which the final pathology revealed a Grade 2 Papillary Serous Carcinoma of the Fallopian tube metastatic to the right common iliac lymph node.

Results: The patient was treated with postoperative "dose dense" Taxol chemotherapy in addition to Carboplatin. Given the lack of survival data and the risk of bleeding and thrombosis Avastin was not added as a therapy.

Conclusions: This a unique case of primary fallopian tube cancer, metastatic to the pancreas and spleen, found in an incidental workup as part of a live liver donor evaluation.
Poster Session III

A RANDOMIZED PHASE 2 STUDY OF TWO DUAL PI3K/MTOR INHIBITORS IN PATIENTS WITH RECURRENT ENDOMETRIAL CANCER

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Background: No standard of care therapy exists for patients with recurrent endometrial cancer (EC) which carries a poor prognosis. Phosphatidylinositol 3-kinases (PI3Ks) constitute a lipid kinase family involved in the regulation of cellular processes, including proliferation, survival, cytoskeletal organization, and glucose transport. Activation of the PI3K/Akt/mTOR pathway is prevalent in EC, and there is emerging clinical evidence that inhibitors of this pathway may be valuable in the treatment of this disease. Inhibitors of mTOR (most of which are analogs of rapamycin) such as temsirolimus and everolimus have been shown to provide modest benefit for the treatment of recurrent endometrial cancer. These observations provide the rationale for development of the dual PI3K/mTOR inhibitors (such as PF-502 and PF-384) in patients with EC.

Study design: This trial is designed to assess the CBR (clinical benefit rate) for both PF-502 (oral) and PF-384 (IV) utilizing a Simon two-stage design for each PI3K pathway activation status (basal vs activated). It is being conducted in women with recurrent endometrial cancer who have had at least one line of platinum containing chemotherapy followed by a recurrence-free interval. Eligible patients will be randomly assigned within each PI3K status to receive either study drug. Stage 1 analysis for CBR will take place after 20 evaluable patients have enrolled on each combination of drug and PI3K status (arm). Prior to advancing arms into Stage 2, all efficacy and safety data will be taken into account. This global trial is open to enrollment and has recruited its first patients.
Poster Session III

CLINICAL STUDY OF AUTOLOGOUS DENDRITIC CELL THERAPY TARGETING MUCIN-1 FOR TREATMENT OF OVARIAN CANCER IN FIRST OR SECOND REMISSION

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Introduction: Cvac™ (Cvac) is an autologous dendritic cell immune stimulant targeting mucin-1 positive tumors.

Objective: CAN-003 is a phase IIb study evaluating Cvac effect on progression free and overall survival in patients with epithelial ovarian cancer (EOC) in remission.

Design: Patients were eligible if they had stage III or IV EOC and obtained a complete response to standard first or second line platinum/ taxane based chemotherapy. The first 7 patients received Cvac to allow evaluation of manufacturing in the US and for safety evaluation. Patients were then randomized either to Cvac therapy or standard of care (SOC). Patients in the active group were treated with up to 10 doses of Cvac, 4 weekly for 7 doses, and 8 weekly for three additional doses.

Results: 63 patients enrolled. Median age was 55 yrs (range 34-75 yrs). Six serious adverse events (SAE) have occurred, four in the Cvac arm (transient hospitalization for bowel obstruction, two hospitalizations for disease progression (one prior to receipt of Cvac and a second related to surgery for disease progression), and febrile neutropenia after docetaxel treatment for disease progression). Two SAE occurred in the SOC (transient hospitalization for bowel obstruction, death due to cerebral hemorrhage). Cvac related adverse events included transient flu-like symptoms, fatigue and mild injection site reactions. Data on progression free survival at one year, and Cvac related T Cell activation will be presented at the meeting.

Conclusion: Study data show that immunotherapy with Cvac is well tolerated. Efficacy data are accruing.
Poster Session III

COORDINATION, FLEXIBILITY AND INDIVIDUALITY PROVIDES HIGH RETENTION RATES

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Background: High retention rates in clinical studies are essential to secure valid data and reduce costs. Aarhus University Hospital, Denmark has included more than 1300 subjects during three years with a minimum of dropouts.

Aim: The aim was: “we want to keep all subjects engaged throughout the study period.”

Methods: Engagement of more than 1300 children, teenagers and women requires various strategies dependent of the scope and structure of each study. Keywords are flexibility and individuality. Every person has an individual approach to participation in a clinical trial.

The study coordination is provided by two full time study nurses and one secretary.

Visiting hours have been adjusted to late afternoons/early evenings. Sessions are successfully run by 10 doctors and 15 nurses and include gynaecological examination, blood sampling, Questions & Answers sessions and individual support. Approximately 180 participants are examined between 4 and 8 PM thus utilizing rooms during out-of-office hours at the hospital.

Recruitment has been successfully conducted utilizing social networks such as Facebook and advertisement in local newspapers. Retention has been achieved by constantly keeping track on the addresses of the participants. We are using the Danish social security number to track “missing” persons.

Results: Having retained in total 1327 out of 1344 persons proves high efficiency and minimal vast of resources.

Conclusions Danish women are interested in participation in clinical trials.

The methods suit the local mentality and behaviour., are cost effective and supports all ages.
Poster Session III

EVALUATION OF A PROSPECTIVE OBSERVATIONAL TRIAL UTILIZING THE CHEMOFX® CHEMOSENSITIVITY AND RESISTANCE ASSAY (CSRA) IN EPITHELIAL OVARIAN CANCER


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Objective: In this study we report clinician practice patterns and demographic and clinicopathologic data from a prospective observational trial (NCT00669422) evaluating the ChemoFx® CSRA.

Methods: 1322 consecutive patients with epithelial ovarian (EOC), fallopian tube (FTCA) or primary peritoneal carcinoma (PPC) with carboplatin/paclitaxel successfully tested were enrolled between 8/2006 and 12/2011. We evaluated common demographic and clinicopathologic factors, and clinical utilization patterns. Assay tested drugs were classified as responsive, intermediately responsive, or non-responsive. Assay compliance was defined as administering a drug scored as responsive or intermediately responsive. Only patients with at least 1 drug scored as responsive or intermediately responsive were evaluated for compliance.

Results: There were 1066 primary and 256 recurrent cases. Patients were mostly white (85%), serous histology (65%), poorly differentiated (71%), and optimally cytoreduced (76%). 15% of primary and 45% of recurrent cases were non-responsive to all agents tested. Compliance rates were 86% for primary cases and 71% for recurrent. Physicians stated ChemoFx affirmed or altered their drug choice 39% and 57% for primary and recurrent cases, respectively. ChemoFx was the primary basis for choice in 28% of recurrent cases. When comparing cohorts, 94% of physicians administered a platinum-containing doublet in the primary and 62% in the recurrent when a patient was considered non-responsive to all drugs tested as compared to 85% in the primary and 41% in the recurrent when patients had variable in-vitro response.

Conclusions: Observations were consistent with published data. Findings suggest physicians incorporate assay results when making clinical decisions in certain cases.
Poster Session III

FEASIBILITY OF ADJUVANT CHEMOTHERAPY AFTER PELVIC EXENTERATION FOR GYNECOLOGIC MALIGNANCIES


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Background: We conducted a pilot study to evaluate the feasibility of administering chemotherapy after pelvic exenteration for gynecologic malignancies.

Methods: We reviewed the medical records of patients who underwent exenterative surgery between 01/2005 and 02/2011. Exclusion criteria included: sarcomatous histologies, patients with ovarian cancer, and patients with follow up < 6 months. Patients were generally referred to chemotherapy based on attending discretion or when high-risk features for recurrence, such as positive margins, positive lymph nodes or LVSI, were present. Treatment regimens consisted of 4-6 cycles of platinum-based doublet chemotherapy. Chemotherapy-related toxicities were assessed using the Common Terminology Criteria for Adverse Events version 4.

Results: We identified 42 eligible patients. Eleven were considered for chemotherapy. Three patients did not receive chemotherapy due to either delayed postoperative recovery or low efficacy concerns. Seven of the remaining 8 patients completed the scheduled treatment. One patient received 3 out of 4 scheduled cycles due to toxicities. Grade ≥2 toxicities were documented in 6 patients (75%). Median follow-up time was 25 months (range, 6-56). The 3-year progression-free (PFS) and overall survival (OS) of patients who did not receive chemotherapy were 35% (95%CI: 16-56%) and 49% (95%CI: 24-69%), respectively. For the 8 patients who received chemotherapy, the 3-year PFS and OS were 58% (95%CI: 18-84%) and 54% (95%CI: 13-83%), respectively.

Conclusions: The administration of chemotherapy is feasible for a select group of patients after pelvic exenteration for gynecologic malignancies. A larger prospective study is required to investigate whether this strategy is associated with a survival benefit.
The aim of this study was to review current literature on total laparoscopic (TLRH) and robot-assisted radical hysterectomy (RRH) with pelvic lymphadenectomy in the treatment of early stage cervical cancer by analyzing data published in individual case series in order to compare surgical and oncological outcomes.

Methods: Up to January 2010, 27 studies were identified that met the inclusion criteria, together with our own unpublished data of patients, accounted for 342 RRH patients and 914 TLRH patients.

Results: There was no statistical difference between the methods in terms of age, BMI or prior abdominal surgery. Estimated mean operative time, blood loss and number of lymph nodes retrieved did not statistically differ between the RRH and TLRH method. Less blood transfusions were needed in patients treated by RRH (5.4%) versus TLRH (9.7%, p< 0.05). Both methods were similar in respect to adjuvant chemo- or (chemo)radiation and recurrence rate. When complications were prioritized to severity, major post operative complications where more frequent in RRH patients (9.6%) than in TLRH patients (5.5%, p< 0.05). The length of hospital stay was significantly shorter in RRH compared to TLRH treatment (3.3 versus 6.2 days respectively; p<0.04).

Conclusions: Robot-assisted and total laparoscopic radical hysterectomy appears to be equally adequate and feasible. RRH studies had small patient populations and further experience beyond the learning curve phase may improve operative time and complication rate. Both minimal invasive techniques should be investigated in a randomized manner.
Poster Session III

UPPER ABDOMINAL RESECTIONS IN GYNAECOLOGICAL MALIGNANCY - THE BARTS EXPERIENCE

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Introduction: In order to improve rates of complete cytoreduction in gynaecological malignancy a team surgery approach has been developed involving hepatobiliary (HPB) surgeons alongside gynaecological oncology (GO) surgeons. We report the procedures and outcomes in patients with gynaecological malignancies undergoing hepatobiliary procedures from 2007 to 2011.

Methods: Case note review was performed for all patients with a gynaecological malignancy where upper abdominal resections were performed. A database was constructed including full operative details, histology, stage and disease status.

Results: 29 patients had combined GO HPB operations. Median age was 57 years (range, 24-70) and follow up was 20 months (range, 1-58). 28(97%) patients had ovarian cancer and 1 endometrial cancer(3%). HPB procedures included: Falciform ligament resection: 16(55%); diaphragm peritonectomy: 11(38%); full-thickness diaphragm resection 8:(28%); splenectomy: 2(7%); partial hepatectomy: 7(24%); cholecystectomy: 6(21%); and porta hepatitis tumour resection, 2(7%). Complete cytoreduction was achieved in 28 patients (97%), 1 patient (3%) had < 1cm residual bowel serosa disease. Four patients (14%) died: One(3%) of post-operative complications at 2 months and three(10%) of disease at 6, 20 and 35 months. Nine (31%) are alive with disease 16(55%) have no disease.

Conclusion: A surgical team approach combining HPB and GO expertise has increased the repertoire of procedures that we can offer GO patients at our institution. This has improved our ability to achieve complete cytoreduction - the most important predictor of survival in advanced ovarian cancer. Long term follow up is needed to assess morbidity and survival in this cohort.
Poster Session III

SURVIVAL AND OPERATIVE OUTCOME ANALYSIS OF ROBOTIC ASSISTED VERSUS LAPAROSCOPIC SURGICAL STAGING FOR ENDOMETRIAL CANCER

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Objective: To evaluate the overall survival outcomes of patients with endometrial cancer managed by robotic and laparoscopic surgery. The second aim was to study the peri-operative outcomes.

Methods: A retrospective study was conducted at two academic centers.

Main outcomes: overall and disease free survival. Secondary outcomes: hospital stay, operative time, blood loss, complications, conversion to open surgery, re-admission and adjuvant therapy. Survival data were estimated using the Kaplan-Meier and Cox regression analysis, and compared using the log-rank test. t-test and chi-squared or Fisher’s exact test was used when indicated.

Results: 404 women met the study criteria. 170 of these had robotic and 234 women had laparoscopic surgical staging. Both groups were comparable in terms of age, body mass index (30 vs. 32), co-morbid medical conditions, previous abdomino-pelvic surgery, histology, and surgical stage. Higher tumor grade was noted in the robotic group.

Median follow-up was 24 months (range 4-43 months) for the robotic assisted group and 57.5 months (range 4 to 103 months) for the laparoscopic group. No significant differences in overall survival (92.9% vs. 92.8%), 2-year disease free survival (90% vs. 93%) and tumor recurrence was found in both groups. Operative time (226 min vs. 181 min), estimated blood loss (109 ml vs. 192 ml) and hospital stay was statistically different (1.9 vs. 2.3 days).

Peri-operative complications and adjuvant radiotherapy was similar in both groups.

Conclusions: Robotic surgery yields equivalent survival results when compared to laparoscopic management for endometrial adenocarcinoma.
Poster Session III

LAPAROSCOPIC UPPER VAGINECTOMY FOR VAGINAL INTRAEPITHELIAL NEOPLASIA AND EARLY VAGINAL CARCINOMA

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Objective: The aim of this study is to describe the feasibility and efficacy of the laparoscopic vaginectomy in vaginal intraepithelial neoplasia (VAIN) and early vaginal carcinoma.

Methods: Three patients with VAIN 2/3, and 1 with early vaginal carcinoma after hysterectomy who have been under laparoscopic vaginectomy between March 2010 and March 2012 were reviewed retrospectively. All the lesions were focally located at upper vagina near stump area. Operative and clinical outcome data were abstracted.

Results: The mean age was 50.7 [range, 40-56] years; the mean operation time was 162.5[145-205] minutes; and the mean estimated blood loss was 55[20-100] ml. The excision pathology is at least $3 \times 3$ cm$^2$ sized. All the patients restituted bladder function after the removal of Foley catheter; the mean hospital stay was 2[1-3] days. One patient with warfarin administration had vaginal stump bleeding, but no other had post operative complication. Three of the patients had no residual lesion, but 1 patient had VAIN 1 in the resection margin. All patients were followed and colposcopy and cytology proved no recurrence.

Conclusion: Laparoscopic upper vaginectomy is feasible and safe in high grade VAIN and early vaginal carcinoma following hysterectomy
Poster Session III

HOMEMADE TRANSUMBILICAL PORT: SINGLE PORT ACCESS (SPA) DEVICE AT A SINGLE CENTER

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Aims: This study aimed to access the safety and feasibility of laparoscopic single port access surgery using a homemade single port device at a single institution.

Materials and methods: Between March 2010 and February 2012, we reviewed data of patients underwent SPA surgery with homemade single port device. An Alexis wound retractor was placed through the umbilical incision and made by fixing a size 7 surgical glove to the retractor ring and securing the glove fingers to the end of 3 trocars (12mm, 11mm, 5mm).

Results: A total of 58 patients have undergone SPA surgery with homemade single port device including SPA-LAVH in 3, SPA-HALS in 13, SPA-adnexal surgery in 42. All SPA surgery with homemade device were successfully completed without any complications. The mean operative time was 108 minutes and median time to achieve the port was 4 minutes. No port-related complications were noted.

Conclusions: The homemade SPA device is safe, effective and feasible. This provides adequate range of motion and flexibility of laparoscopic instrument.
Poster Session III

A HELPING HAND WITH LEPAND: TIPS FOR LAPAROSCOPIC EXTRA-PERITONEAL PARAORTIC NODE DISSECTION IN MANAGING LOCALLY ADVANCED CERVICAL CANCER

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Introduction: Laparoscopic extra-peritoneal para-aortic node dissection in locally advanced cervical cancer identifies those patients with micro metastases and allows for individualization of radiation treatment. This approach has been adopted as a standard in our institution. The extra peritoneal approach is felt to minimize the morbidity of the procedure, however it remains a challenging technique even for the experienced surgeon. Particular issues are the intricacies of dissection on the Caval-right side of the field and the difficulties encountered if an inadvertent defect in peritoneum is made.

Objective: Through our experience of over 100 cases we have developed experience in 'trouble-shooting' techniques. We aim to demonstrate by means of high definition video footage and with pictorial references our various techniques for overcoming various intra-operative difficulties.

Materials and methods: 'Live' high definition video footage and pictorial guidance to performing extra peritoneal para aortic node dissection

Results: Demonstration of the use of an inflatable balloon inserted extra-peritoneally via a trocar that acts to occlude defects in the peritoneum, thereby allowing pressures to be maintained and operating to continue, with minimal disruption to the operating field.

Comparison of the different views obtained using a 30 degree laparoscope, allowing better appreciation of the anatomy and facilitating dissection on the caval side by 'seeing over the top' of the aorta with minimal counter traction and manipulation.

Conclusion: We demonstrate simple, yet safe and effective techniques for optimizing the operative field during laparoscopic extra peritoneal para-aortic node dissection.
Poster Session III

EVALUATION OF SURGICAL SIMULATION USING THE DA VINCI ROBOT SKILL SIMULATOR

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Introduction: The primary objective of this study was to determine if there is a difference in performance on the da Vinci® Robot Skill Simulator based on the participant's level of training. The secondary objective was to assess the validity of the simulator as an educational platform in surgery.

Methods: The da Vinci® Robot Skill Simulator scored exercises based on a set of metrics. Participants included medical students, residents, fellows and staff from the Division of Gynecology Oncology. Participants were given a questionnaire to assess the importance of the simulator in surgical training.

Results: Three staff gynecology oncology surgeons, 4 fellows, 17 residents, 13 medical students, and 4 other participants completed simulation exercises during the study period. Based on the mean exercise scores of first attempts, staff, fellows and senior residents scored better compared to junior residents, medical students, and other participants. This trend disappeared once the participants used the simulator for 5 exercise attempts. The questionnaire revealed that the simulator was realistic (mean=8.1/10), was useful for residents (mean=9.5), and should be included in robotic training (mean=9.7). The participants felt that the ideal mean total robotic training time for junior residents, senior residents and fellows should be 36, 26, and 22 hours respectively.

Conclusions: There is a trend for senior residents, fellows and staff to initially score better on the simulator. The trend disappeared once all participants gained experience. Robotic surgical simulation might become an important educational tool as robotic-assisted surgeries continue to gain momentum across many surgical specialties.
Poster Session III

SINGLE PORT ACCESS (SPA) ROBOT ASSISTED LAPAROSCOPIC SURGERY FOR PATIENTS WITH OVARIAN TUMOR LOW MALIGNANT POTENTIAL (LMP’S): FARGHALY’S TECHNIQUE

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Low malignant potential (LMP’s) ovarian tumors account for 10% to 15% of all ovarian epithelial tumors. Patients with LMP’s exhibit the following characteristics: a younger age at time of diagnosis, an earlier stage at time of presentation, a longer survival rate, and late recurrences. The survival rate in those patients is 98% to 100%. It is important to for these patients to preserve fertility. All patients undergo preoperative blood testing, and contrast-enhanced multi-sliced CT. All patients undergo bowel preparation prior to surgery. Da Vinci surgical system is used. An intrauterine device is used to mobilize the uterus. A 2-cm intraumbilical vertical skin incision and a 2.5-cm rectus fasciotomy are performed to enter the peritoneal cavity. A single port trocar with 4 integrated access ports is used and inserted into the abdominal cavity, and the abdomen is insufflated to 12 mm Hg. The patient is then put in a Trendelenburg position. Salpingo-oophrectomy is performed on the affected side of the ovary and fallopian tube. Then the robot is unlocked, and the skin incisions are sutured. Operative time can be maintained in 45 minutes, mean blood loss of 100 ml, and hospital stay for 3 days. Farghaly’s Technique of single port access robot assisted laparoscopic unilateral salpingo-oophrectomy for LMP’s ovarian tumors is safe, feasible, cost effective, with acceptable operative, pathological and short and long term clinical outcome. It retains the advantage of minimally invasive surgery. SPA surgery offers, reduction of operative complications, less postoperative pain, and better cosmetic results.
Poster Session III

COMPARISON OF PERIOPERATIVE AND CLINICAL OUTCOMES IN THE MANAGEMENT OF EPITHELIAL OVARIAN CANCER: ROBOTIC VS. ABDOMINAL APPROACH

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Objectives: To evaluate the feasibility and efficacy of robotic-assisted management of epithelial ovarian cancer and to compare perioperative outcomes to an abdominal approach.

Methods: Retrospective chart review of epithelial ovarian cancer cases managed with either robotic-assisted or abdominal surgery by a single surgeon between 2008 and 2011. Cases included those presenting with pelvic mass, initial staging, or debulking after neoadjuvant chemotherapy.

Results: There was an increase in the use of the robotic approach, from 27% in 2008 to 100% in 2011 (p< 0.001), with a corresponding decrease in the use of an abdominal approach. Overall, 42 patients underwent a robotic approach and 23 patients underwent an abdominal approach.

Patient characteristics were similar for age (Robotic 59.0 yrs vs. Abdominal 54.4 yrs, p=0.1322), and prior abdominal surgery (R 66.7% vs. A 87.0%, p=0.086). On average, patients in the robotic group had a higher BMI (39.9 kg/m² vs. 28.0 kg/m², p < 0.0001), longer operative time (126 min vs. 95 min, p=0.0015), and less blood loss (73 cc vs. 391 cc, p< 0.0001). The average hospital stay was significantly shorter in the robotic group (1.25 days vs. 6 days, p< 0.0001). There was no residual disease in 85.7% of robotic patients and 56.5% of abdominal patients (p=0.02). In Stage III survival data favored the robotic group (R 82% vs. O 64%).

Conclusion: The use of a robotic approach in the management of epithelial ovarian cancer is feasible and effective. Optimal debulking and survival rates are similar to the traditional open approach.
Poster Session III

ROLE OF RADICAL SURGERY IN MANAGEMENT OF TRAUMATIC UTERINE ARTERIOVENOUS MALFORMATION

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Introduction: Traumatic arteriovenous malformations (AVM) can develop after uterine instrumentation. The increased risk of vascular changes, including abnormal placentation, after repeated cesarean sections, is well-studied. We report a case of a patient with delayed near-exsanguination from a uterine AVM, following dilation and curettage for a cesarean scar ectopic.

Case report: A 32-year-old G3P2 presented in August 2011 with a cesarean scar ectopic, which was treated with dilation and curettage, incurring a 1500ml blood loss. Within 6 weeks, she returned with two episodes of heavy vaginal bleeding. Initial angiography was interpreted as a high-flow AV fistula, which was coiled. Vaginal hemorrhage recurred; repeat angiography demonstrated a large AVM.

Gelfoam embolization of the bilateral internal iliac arteries reduced vascularity of the AVM by 40-60%. The AVM location at the left lateral apex of cesarean scar extending into the parametria necessitated a radical hysterectomy to ligate the uterine arteries at the origin. A ureteral dissection with unroofing of the ureteral tunnel to dissect around the AVM was necessary to complete surgery.
Conclusions: The prevalence of uterine AVM has increased with the rise in surgical obstetrics. In the patient with a failed prior interventional procedure, surgical management is necessary to prevent life-threatening hemorrhage. Location of AVM within the abnormal scar of uterine tissue requires familiarity with radical pelvic surgery to definitively treat this delayed obstetrical complication.
Poster Session III

THE ROLE OF TRANSPLANT SURGICAL SERVICES IN GYNECOLOGIC ONCOLOGY PATIENTS AT A UNIVERSITY TERTIARY REFERRAL CENTER

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Objectives: To report the clinical utility of Transplant service in Gynecologic Oncology.

Methods: Retrospective cohort of all new Gynecologic Oncology patients seen over one year period.

Results: 708 patients were referred for possible gynecologic malignancies, leading to 325 major surgeries. Endometrial cancer n= 72 and ovarian tumors n=120 (60 optimal debulking). Of those, 5 patients (0.7%) were referred to the organ transplant service. Two patients were considered for intestinal transplantation following grade 4 radiation enteritis: adjuvant radiation for stage IIIC2 endometrial cancer and primary radiation therapy for advanced cervical cancer stage IIA. Three patients with advanced ovarian cancer were referred for apparently"non-resectable"disease. Two patients were deemed resectable but not otherwise candidates due to medical comorbidities. One patient had an invasive atypical borderline tumor that recurred in the small bowel mesentery. She was scheduled to autologous small bowel transplant, with removal of the small bowel, followed by resecting the tumor and re-anastomosis of the ex-vivo small bowel. The tumor was found to be unresectable with diffuse mesenteric disease involving all potential blood vessels for reanastomosis.

Since initiating autologous transplant for resection of neoplasm, the Transplant service managed 14 patients including 2 from hospice. Thirteen received multivisceral organ transplant and 1 received an isolated intestinal transplant. The majority was neuroendocrine tumors and 3 were desmoid tumors.

Conclusion: Consultation with Transplant Surgery service was uncommon in Gynecologic Oncology; however Transplant Surgery contributed an important role in the management of solid tumors. Gynecologic Oncology may be an area for collaboration with Transplant Surgery.
Poster Session III

OVARIAN SURVIVAL AFTER PELVIC RADIATION: THE EFFECT OF AGE AND OOPHOROPEXY

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Introduction: Published rates of ovarian survival (OS) and complications after ovarian transposition (OT) differ greatly. At the Leiden University Medical Center we conducted a retrospective control study to evaluate the ovarian function after OT and pelvic radiation and the effect of age.

Materials and methods: Group 1 consisted of women who underwent OT prior to pelvic radiation. The control group consisted of women, diagnosed with cervical cancer and treated with hysterectomy/trachelectomy and radiation therapy. All women were < 45 years and treated between 1989 and 2011. The 5 year OS rate was calculated, with a sub-analysis for age (25-30; 31-35 and 36-40 years).

Ovarian failure was defined as climacteric complaints (with or without starting hormone replacement therapy) and/or laboratory measurements (FSH>40 IU/L and/or estradiol < 100 pmol/L), or bilateral salpingoophorectomy. Women were censored at recurrence.

Results: Twenty-seven women after OT and 29 controls could be included (mean age at radiation respectively 33,4; range 25,20- 44,6 and 36,7; range 25,9-44,3). The radiation dose was 44,8Gy (25,0-63,0Gy) and 46,3 Gy (45,0-50,0Gy) respectively.

The 5 years OS rate was 51,0% (SE 14.1%) versus 0% (p=0.000).

The 5-year OS of 3 different age groups (25-30; 31-35 and 36-40 years), was respectively 87.5% (SE 11.7%); 47,6% (SE 22,5%) and 28,6% (SE 17,1%) (after OT only).

Conclusions: OT in premenopausal women is an effective procedure to reduce the time to premature ovarian failure caused by RT: 5 yr ovarian survival 51% vs 0%. Ovarian survival increases with younger age which allows age dependent prediction models.
Poster Session III

MINIMAL ACCESS SURGERY FOR INTERVAL CYTOREDUCTION IN OVARIAN CANCER

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I. Position: Lithotomy with sandbag under pelvis. Legs put in straight stirrups. Surgeon stands on the right side of the patient.

II. Placement of ports: Camera Port - 10mm metal port approx 1-2cms above umbilicus in midline. Port placed by open technique. Entire abdomen checked & operability assessed.

Ports on right side:
1st: 12mm - At McBurney's point.
2nd: 5mm - Triangulate between camera port & Rt. Side 12mm port.

Ports on left side:
1st: 5mm In left iliac fossa, mirror image of Rt. Side 12mm.
2nd: 10mm, Triangulate between camera port & Left side port in Left Iliac Fossa.

III. Hysterectomy: Uterus held with a 10mm claw forceps through Lt. side 10mm port. Simple hysterectomy done with bilateral salpingo-oopherectomy and peritonectomy if needed. Specimen retrieved per vaginum.

IV. Omentectomy: Surgeon stands between the patient's legs Camera, through right side 12mm port, Pt. head end up. Surgeon operates through the right side 5mm & left 5/10mm ports. Omentum held through supraumbilical & left 5mm port. Total omentectomy done from right side of transverse colon along its entire length. Then remaining just distal to Gastroepiploic arcade, supracolic omentum dissected along stomach. Omentum is freed & retrieved per vaginum.

Vault of vagina closed with intracorporeal sutures using 2-0 PDS / Quill. Haemostasis secured, counts tallied. No.28 tube drain placed in pelvis through left side 5mm port. 12 & 10mm ports closed with a suture passer.
Poster Session III

A COMPARISON OF LAPAROSCOPIC AND ABDOMINAL RADICAL PARAMETRECTOMY FOR CERVICAL STUMP CARCINOMA AFTER HYSTERECTOMY

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Design: Observational study (Canadian Task Force classification II-2).

Patients: Forty consecutive patients indicative for RP.

Intervention: Twenty-two and 18 underwent ARP and LRP, respectively.

Measurements and main results: Information was collected on demographics, indications for initial and this surgery, tumor characteristics, intra- and post-operative parameters and complications. The lengths of resected parametrial and vaginal tissues were measured. Compared with ARP, LRP resulted in shorter operative time, less blood loss, shorter hospital stay, and removed more pelvic lymph nodes. ARP had 1 case of injury to the small intestine during operation while LRP had 1 urethral/vaginal fistula after surgery.

Conclusion: LRP is superior to ARP in terms of shorter operative time, less blood loss, and shorter hospital stay while maintaining the completeness of the procedure. It can be safely performed in the hands of experienced surgeons for cervical or vaginal apex carcinoma and stage II endometrial cancer after hysterectomy.
SKIN BRIDGE LOOP STOMA IN A GYNECOLOGIC ONCOLOGY UNIT

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Bowel obstruction, perforation and fistulisation are not uncommon events in gynecological cancer patients. Surgical diversion is undertaken urgently for perforation and fistulisation and usually after a failed trial of conservative management. Loop stoma is preferable to end stomas for patients with poor performance status. Elevation of bowel in the presence of fibrosed or carcinomatous mesentery over a rigid support is sometimes challenging and post-operatively there could be delays in self-care and complications eg stomal infection and retraction. We adopted the skin bridge technique initially described for colostomy by Jarpa (1986) to loop ileostomy and colostomy in our service.

Objective: To determine the safety and feasibility of the skin bridge loop technique for colostomy and ileostomy. A prospective observational case series of all skin bridge loop stoma formation in a tertiary gynecological oncology unit in Ireland from October 2010 to February 2012.

Method: The skin is dissected to create a central narrow skin bridge. The skin bridge is divided to create two skin flaps of unequal length. Dissection is carried downwards and the intestinal loop is delivered. The longer skin flap is pulled through a fenestration in the mesentery and the skin ends are sutured together with monofilament non-absorbable 2/0 suture. The stoma is matured with interrupted monofilament absorbable 3/0 sutures.

Results: No stomal complications arose in our case series in follow-up to 73 weeks. Stomal education was commenced from the first postoperative day and self care was achieved in a median of 5 days. We recommend this technique in Gynecologic Oncology.
Poster Session III

SURGICAL ANATOMY OF THE COMMON ILIAC VEINS IN PARA-AORTIC LYMPHADENECTOMY FOR GYNECOLOGICAL CANCER

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Objective: It is a well-known etiology that the compression of the left iliac vein between the right iliac artery and the vertebrae is associated with a predominant occurrence of left iliofemoral deep venous thrombosis (DVT). In this study, we studied surgical anatomy and compression of the common iliac veins during live operations for gynecological cancers.

Methods: The anatomical variation and the compression of left iliac veins were identified in 100 patients who underwent systemic para-aortic lymphadenectomy at the time of surgery for gynecological cancers. Their medical records were reviewed with respect to patient-related, disease-related and surgery-related data.

Results: The degree of iliac venous compression was classified into three grades: Grade A (n = 20), with calculated percentage of 0-20%. Grade B (n = 37), with calculated percentage of 21-50%. Grade C (n = 38), with calculated percentages greater than 50%. Five patients had left iliac vein with anomalous appearances; 3 with small caliber vessels and 2 with double inferior vena cava. Correlations between the degree of iliac venous compression and the quantity of D-dimer level or the presence of DVT could not be noted.

Conclusions: To know the variability in vascular anatomy of the iliac veins may be useful for surgeons to accomplish para-aortic lymphadenectomy in safety.
Poster Session III

SENTINEL LYMPH NODE BIOPSY IN EARLY VULVAR CANCER - THE GLASGOW EXPERIENCE

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Background: Management of early stage vulval cancer involves surgical excision of the primary tumour with or without surgical removal of groin nodes. Only 25-30% will have positive nodes making remainder unlikely to benefit from a procedure which has significant short and long term morbidity.

Aim: To report our experience of SLNB in early squamous cell vulval cancer.

Methodology: Suitable cases of vulval cancer discussed at MDT meetings between 2002 and February 2010 were offered SLNB.

Results: 32 cases underwent SLNB. 56.3% were G2. The mean depth of invasion was 3.27 mm (range 1-21). 87.5% had background pathology. 12 had unilateral and 20 had bilateral SLNB. A total of 160 lymph nodes were removed (mean 5, range 1-12). There were only 3 cases with positive SLN (9.4%). 2 had completion inguino-femoral lymphadenectomy, while another had combined chemo-radiation.

Cumulative follow-up was 1430 months (mean 47.7, range 5-116). There were 2 cases of true relapse in the groin (6.3%). One other developed a new vulval primary with positive groin node. There were 3 cases with wound infection/delayed healing and one case with lymphocyst. There were no cases of chronic lymphoedema in those who did not also receive adjuvant therapy/formal groin node dissection.

Conclusion: In our group follow up is longer compared to the large multicentre trial by Van der Zee et al¹ and may explain the higher recurrence rate. We believe that global adoption of SLNB should be deferred until further large multicentre trials evaluate in particular, its long term safety.

References:

Poster Session III

PATHOLOGIC ANALYSIS OF TISSUE DESTRUCTION WITH NEUTRAL ARGON PLASMA

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Introduction: Many electrosurgical devices and lasers have been developed over the years to aid tissue dissection and destruction. Each device has specific applications with advantages and disadvantages. Lateral thermal spread(LTS) and collateral tissue destruction(TD) are the principal concerns when considering a new operative energy source.

Objective: This study reports the histopathological effects of TD following neutral argon plasma(PJ) use on fresh ex-vivo human benign and malignant tissues including at different power settings, tissue interaction time examining depth of destruction and LTS.

Methods: Following consent, fresh tissue was harvested intra-operatively. Following tissue excision, 1cm³ sections of tissue was exposed to PJ at 4 power settings (20%,40%,60%,80%) and increasing time of exposure ranging from 1-5seconds. Power is expressed stepwise as a percentage (10-80%) on the PJ.Specimens were formalin-fixed and stained after PJ exposure. Histological examination of TD included assessment of cavity depth and extent of burn at the base of cavity (eschar) is used as a surrogate marker of LTS.

Results: TD increased with power setting and ranged from 0.8 mm at (20%) to 2.95 mm at 80%. However, depth of eschar remained fairly constant despite increasing the power(0.12-0.20mm). Duration of tissue exposure appeared to be more important than increasing power settings.

Conclusions: PJ is a safe device that may be used on various tissue surfaces. Extent of tissue vaporisation produced is dependent upon both power settings and duration of exposure. However, increasing these parameters did not seem to impact on lateral thermal spread making the PJ an attractive electrosurgical device.
COMPLETE CYTOREDUCTION OF OVARIAN MALIGNANCY USING NEUTRAL ARGON PLASMA

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Background: “Optimal cytoreduction” (<1cm) is associated with increased survival and disease free interval for epithelial ovarian malignancy (EOC) with best results following complete resection. PlasmaJet™ (PJ), a new device producing a jet of argon plasma by heating argon gas may be used to vaporise small tumour nodules.

Aim: Evaluate the feasibility and outcome of conversion from optimal cytoreduction of recurrent disease (<1cm) to microscopic disease only in laparoscopic surgery.

Materials & methods: Prospective study in tertiary gynae-oncology centre. PJ used in 17 open and 8 laparoscopic debulking procedures.

Patient demographics, intra and post-operative data collected. Size/location of pre-surgical disease, procedures performed, tissue and anatomical location subjected to PJ, power settings and time taken to ablate tumour deposits recorded.

Results: PJ used to treat peritoneal deposits of EOC metastases on serosal surface of small and large bowel in 12/17 cases and treat deposits on the serosal surface of the liver, diaphragm and peritoneal undersurface of the pericardium with no adverse affects in 3/25. Laparoscopic ablation of diaphragmatic deposits, pericardial pericardium carried out using PJ in 3 cases. Disease on liver surface and diaphragmatic nodules resected with no visible disease.

Conclusion: Preliminary data on feasibility and safety are reported suggesting that PJ is an innovative surgical device with several features well suited for the destruction of EOC implants and tumour plaques.
Poster Session III

ROBOTICS IN GYNAECOLOGICAL ONCOLOGY - THE GUILDFORD EXPERIENCE

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Introduction: Uptake of laparoscopic surgery among gynaecologists has been surprisingly poor with only 14% reduction in open surgery, due to the long learning curve to acquire the necessary advanced laparoscopic skills. We report our experience of introducing robotic surgery (RS) for endometrial (EC), cervical (CC) and ovarian cancer (OC).

Materials and methods: Prospective observational study in a gynaec-oncology centre with 2 surgeons over 2 years. Patient demographics, intra and post-operative data recorded.

Results: 125 Cases performed. The case-mix included (39) CC, (73) EC and (9) OC and 4 benign causes. BMI ranged from 17-59 (Mean 33; Median 32). Median estimated blood loss overall was 50mls (5-2500). Median hospital stay was 1 day. Lymph node yield was comparable (20-56). Despite being skilled laparoscopic surgeons 64.5% of these cases would not have been offered laparoscopic surgery in our institution often due to morbid obesity.

Conclusion: RS certainly has a role in gynaecological oncology due to the precision and the mechanical advantages it confers. Set-up costs and maintenance are expensive but ongoing costs are similar to laparoscopic surgery. Advantages to patients include reduced blood loss, post-operative pain, shortened hospital stay with minimal requirements for transfusion and HDU/ITU post-op. Advantages to surgeons include autonomy of camera control, 3D-HD image leading to greater appreciation of anatomy and improved ergonomics.

These translate into many more women benefitting from MAS for their gynaecological cancer with reduced risk of infections and TED. Adoption of RS would enable smaller cancer centres to offer patients MAS as large surgical teams are not require
Poster Session III

LAPAROSCOPIC RETROPERITONEAL LYMPHADENECTOMY IN GYNAECOLOGICAL CANCER

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Introduction: To evaluate the feasibility and effectiveness of laparoscopic retroperitoneal lymphadenectomy in gynaecological cancer.

Study design: We present a video showing the steps of retroperitoneal lymphadenectomies based on 35 cases performed in Institut Universitari Dexeus from 2007 to 2011. The following data were reviewed: pathological data and postoperative follow-up (length of hospital stay, blood loss).

Results: The mean age was 55.2 years. 50% of tumors were endometrioid type endometrial carcinoma, 16.6% papillary serous endometrial carcinoma, 16.6% cervical carcinoma, 5.5% carcinosarcoma, 2.22% ovarian cancer. The number of aortic lymph nodes analyzed varied from 4 to 29 (mean 13.11) A single retroperitoneal aortic lymphadenectomy was performed in 22% and an hysterectomy with both pelvic and aortic lymphadenectomy in 77.78%. Operating time was 161.25 minutes in a single retroperitoneal aortic lymphadenectomy and 243 minutes when hysterectomy and pelvic/aortic lymphadenectomy were performed. The mean drop in haemoglobin in single aortic lymphadenectomy was 1.22 compared to 1.69 in the hysterectomy group. The mean length of hospital stay was 4 days. Blood transfusion was not required. There were no intra-operative complications but 3 cases presented minor postoperative complications: deep vein thrombosis in lower extremity, lymphocele and wound infection.

Conclusions:

- Lower rate of intestinal adhesions and complications.
- Reduced hospital stay and shorter recovery time.
- Do not delay the onset of adjuvant radiotherapy or chemotherapy.
- It requires a learning curve for the surgeon and the standardization of the technique.
Poster Session III

SURGICAL DIATHERMY INDUCED TUBAL INJURY MAY AFFECT DETECTION OF OCCULT TUBAL LESIONS IN HIGH-RISK WOMEN UNDERGOING RISK REDUCING SALPINGO-OOPHORECTOMY (RRSO)

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Background: Electro-surgery induced tubal thermal injury obscures cellular detail and hampers histomorphological assessment for occult pathology.

Objective: To report on diathermy related thermal injuries to the fallopian tube observed at RRSO and explore its potential impact on the detection of occult tubal epithelial lesions.

Design: High-risk women from breast and/or ovarian cancer families attending a tertiary high-risk familial gynaecological cancer clinic. Retrospective case control analysis of high-risk women who underwent RRSO. Cases: All women detected to have occult lesions (tubal atypia/carcinoma in situ/cancer) between January-2005 and December-2010. Controls: All women with normal tubal/ovarian histology between August-2006 and December-2007.

Methods: Two pathologists performed histopathological assessment for grade of thermal injury. Tubal diathermy injury rates were compared between cases and controls. Statistical analysis was undertaken using SPSS-18. The Mann-Whitney test compared age distributions, Chi-Square / Fisher's tests the difference between proportions and Gamma test the difference in ordinal variables between the groups.

Results: A novel tubal thermal index describing the severity of thermal injury is reported. Lack of fimbrial thermal injury is twice as likely (odds ratio 2.04, 95%CI 1.06,3.92) to be associated with detection of occult tubal pathology, whereas isthmic injury does not affect detection rate (p=0.744). The groups were comparable with respect to age at RRSO (p=0.531) and the presence of BRCA mutations (p=0.192).

Conclusions: This report highlights the potential impact of electrosurgical thermal injury on detection of occult tubal pathology following RRSO. It is important for surgeons to avoid thermal injury to the distal end of the tube.
Poster Session III

ROBOTIC SURGERY FOR ENDOMETRIAL CANCER: HOW TO REDUCE COSTS

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Introduction: Robotics surgery has many advantages but cost is still the main limit for the diffusion of this technology. The objective of this study was to analyse the feasibility to reduce costs in case of robotics surgery for endometrial cancer.

Material and methods: 22 endometrial cancer patients, undergoing robotic surgery at CFO, were enrolled in the study from June 2010 to April 2012. Data on patients, tumour’s characteristics, kind of surgery, operative times, complications, conversion and costs related to operating room (OR), hospital, laboratory and pharmacy fees were prospectively recorded in a computed database. Surgeries were divided in two different robotics approaches in relations to numbers of operative robotic arms, OR staff composition, disposable and non-disposable instruments. Comparison of costs and feasibility between the two groups was performed.

Results: 8 patients were treated following the standard robotic approach (A) with 4 robotic arms and 14 women with the modified approach (B) with 3 robotic arms, reduction of disposable instrumentation and OR staff. Pelvic lymphadenectomy was performed in 14 cases (5 in group A and 9 in group B). Median operative time group A: 214 minutes (range 157-265), group B: 185 minutes (range: 126-219). No intra-operative or post-operative major complications occurred in both groups. Median hospital cost per intervention (excluding robotic surgical system cost) was in group A: 8,858 Euros and in group B: 7,244 Euros with a reduction of 18%.

Conclusion: The present study demonstrates the possibility to reduce costs of single robotic surgery thanks to a modified approach.
Poster Session III

LAPAROSCOPIC SINGLE PORT EXTRAPERITONEAL PARA-AORTIC LYMPHADENECTOMY

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Background: Single-incision laparoscopy is an emerging concept that offers excellent cosmetic results. The authors present the video about extraperitoneal para-aortic lymphadenectomy performed by single port laparoscopy in case of bulky lymph nodes.

Method: A 56 years old woman, affected by squamous carcinoma of the cervix, FIGO stage 1B2, with bulky common iliac and para-aortic lymph nodes at TC scan, underwent extraperitoneal para-aortic lymphadenectomy. A 2 cm incision was made 2 cm above the traditional incision point described by Querleu, surgeon’s index finger was inserted to bluntly develop the retroperitoneal space. X-cone reusable single-port device was positioned and insufflations of 12 mm Hg of C02 gas performed. 5 mm, 30-degree laparoscope was placed into the right channel, curved atraumatic S-portal forceps into the left access and harmonic scalpel into the central channel. After retroperitoneal identification of psoas muscle, iliac vessels, and ureter, blunt dissection of the adventitial tissue was performed till the identification of the left renal vein. Lymphadenectomy specifically targeted the left-sided supra and infra-mesenteric para-aortic spaces to remove bulky lymph nodes detected by CT scan.

Results: Operation was performed successfully with no intra-operative or postoperative complications. Operative time was 165 minutes. 9 lymph nodes were removed, no metastasis were detected. Dietary intake was started in day 0. Patient was discharged on day one.

Conclusion: This report suggests that, in experienced hands, single port extra peritoneal para-aortic lymphadenectomy in case of bulky lymph nodes is feasible without particular differences in term of anatomic exposition and technique from the multi-access approach.
Poster Session III

A NEW TECHNIQUE FOR KNOTLESS CLOSURE OF THE VAGINAL CUFF DURING ROBOTIC HYSTERECTOMY USING A WELDED LOOP UNIDIRECTIONAL BARBED SUTURE

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Objectives: To assess the safety and efficacy of using a unidirectional barbed suture to accomplish a knotless vaginal cuff closure during robotic hysterectomy.

Methods: All patients undergoing robotic assisted total hysterectomy from July 1, 2010 to July 1, 2011 were included in this IRB approved analysis. Providers utilized either a 2-0 synthetic absorbable suture to close the vaginal cuff in a running fashion, secured with an absorbable suture clip at the angles and then knotted in the middle or 2-0 unidirectional barbed suture with a welded loop closure. Demographic characteristics, surgical details, pathology, method of cuff closure, and post operative complications were collected.

Results: 2-0 tied synthetic absorbable suture was used in 58 patients while 2-0 welded loop knotless closure was used in 76 patients. No patient experienced vaginal cuff dehiscence or cellulitis. Rates of vaginal spotting or bleeding were comparable in both groups (12% in 2-0 monofilament absorbable suture vs. 13% in 2-0 absorbable barbed suture). All vaginal cuff bleeding resolved on its own without significant intervention. Patient demographics including mean age, BMI and postoperative complications were similar among the two groups. Over the course of 12 months all five attending surgeons switched to the knotless closure.
Conclusions: The use of a single 2-0 absorbable welded loop unidirectional barbed suture to close the vaginal cuff in a running fashion is safe and well tolerated. The unidirectional barb precisely secures the tissue at numerous points and evenly distributes the closure forces allowing for a fast, knot free vaginal cuff closure.
AUTOAMPUTATION OF THE ADNEXAE DUE TO TORSION OF PREVIOUS OVARIAN CYST

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\textbf{Background:} Torsion of adnexa usually is manifested with severe abdominal pain and is treated as an acute surgical emergency. Amputation of an ovary by previous torsion, and sometimes with other adnexal structures as well, are extremely rare.

\textbf{Case:} A 61-year-old Korean woman complained of dull intermittent lower abdominal pain for 2 years. She was referred to us for presumed uterine tumor. Pelvic examination, ultrasonography and abdominal computer tomography imaging revealed a various size of multiple myoma, and her serum CA125 and CA19-9 was normal respectively, because of movable abdominal pain, laparoscopy was performed. In front of uterus, the patient was found to have a mass with no ligamentous or direct connection with the pelvic organs. The right ovary and tube was absent. She had no operation history.

These findings were interpreted as an autoamputation of the adnexae due to torsion of previous ovarian cyst arising from the right ovary.

\textbf{Conclusion:} Physicians should bear in mind the possibility of an autoamputated ovarian cyst even if the preoperative radiograph shows no calcification.
Poster Session III

SINGLE-PORT VERSUS CONVENTIONAL LAPAROSCOPIC SURGICAL STAGE FOR EARLY-STAGE ENDOMETRIAL CANCER


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Objectives: To analyze the feasibility, safety, and efficacy of single-port laparoscopic surgical staging for early-stage endometrial cancer compared to conventional laparoscopic surgical staging.

Methods: Prospective cohort consisted of consecutive 15 patients with low risk early-stage endometrial cancer who underwent single port laparoscopic surgical staging including hysterectomy, bilateral salpingo-oophorectomy (BSO) and pelvic lymph node dissection (PLND) comprised a study group. Consecutive 30 patients with low risk early-stage endometrial cancer who underwent four-port laparoscopic surgical staging including hysterectomy, BSO and PLND before the study period comprised a control group. Surgical outcomes were compared between the two groups.

Results: No one in the single-port and four-port group required additional trocar or conversion to laparotomy. There were no between-group differences in mean age, menopause, parity, body mass index, and previous history of abdominal surgery, nor were there between-group differences in the number of lymph nodes retrieved (single-port vs. four-port, 30.5 vs. 26.3, P = 0.141), the operating time (177 min vs. 161 min, P = 0.288), estimated blood loss (189 mL vs. 181 mL, P = 0.786), perioperative hemoglobin level change, transfusion, postoperative hospital stay (4.6 days vs. 5.1 days, P = 0.290), and perioperative complications (0% vs. 3.3%, P > 0.999).

Conclusion: Single-port laparoscopic surgical staging including hysterectomy and PLND was feasible and safe in patients with low risk early-stage endometrial cancer. It could be an effective surgical management for these patients. Further evaluation of single-port laparoscopic surgical staging in a prospective randomized trial is required.
Poster Session III

ROBOTIC RADICAL HYSTERECTOMY IN EARLY-STAGE CERVICAL CARCINOMA PATIENTS, COMPARING RESULTS WITH LAPAROSCOPICALLY ASSISTED RADICAL VAGINAL HYSTERECTOMY CASES

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Objective: To compare intraoperative, pathologic and postoperative outcomes of robotic radical hysterectomy (RRH) to laparoscopically assisted radical vaginal hysterectomy (LARVH) in patients with early stage cervical carcinoma.

Methods: The first twenty patients with cervical cancer stages IA2-IIA underwent RRH and were compared with previous twenty LARVH cases. The procedures were performed at University Hospital Olomouc, Czech Republic between 2004 and 2011 by two surgeons (P.R., D.P.).

Results: There were no differences between groups for age, body mass index, tumor histology, stage, lymphovascular space involvement or nodal status. No statistical differences were observed regarding operative time (265.4 vs 295.2 min). The mean (SD) estimated blood loss (EBL) was 143.3 ml in RRH group and 352.5 ml in LARVH. This difference was statistically significant in favor of RRH group (p=0.0001). Mean length of stay was significantly shorter for the RRH group (7.2 versus 8.6 days, p=0.02). Mean pelvic lymph node count was similar in the two groups (20 vs 21). None of the robotic or laparoscopic procedures required conversion to laparotomy. The differences in major operative and postoperative complications between the two groups were not significant.

Conclusion: Based on our experience, robotic radical hysterectomy showed better results than traditional laparoscopically assisted radical vaginal hysterectomy in early stage cervical carcinoma cases. We feel the intuitive nature of the robotic approach, even during the learning curve, combined with significant reduction in surgeon’s fatigue offered by the robotic system will allow more surgeons to use a minimally invasive approach to radical hysterectomy.
Poster Session III

THE TECHNICITY INDEX: A USEFUL PERFORMANCE INDICATOR FOR MINIMALLY INVASIVE SURGERY IN ENDOMETRIAL CANCER AND GYNECOLOGIC ONCOLOGY

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Introduction: Minimally invasive surgery (MIS) is the surgical approach of choice for the management of numerous non-oncologic and oncologic conditions. The Technicity Index (TI) is defined in this study as the ratio of minimally invasive hysterectomies compared to abdominal hysterectomies during the studied time period. It indicates, in this context, a higher performing surgical technique and can thus be used as a healthcare indicator. The objective of this study was to evaluate if the TI from three different time periods had significantly increased with regards to the surgical management of endometrial cancer in our gynecologic oncology division.

Methods: The TI was calculated from the data of the OPERAÔ surgical management system from July 1999 to June 2011. The study period was divided into 3 equal time periods (P1:1999-2003; P2: 2003-2007; P3:2007-2011). The z-score was used with a 0.05 level of significance.

Results: The TI of the 2 first time periods were comparable (p= 0.96), however the differences between each of the first 2 time periods compared to the last one (P1 vs P3 and P2 vs P3) were statistically significant with p values of < 0.001 and 0.00016 respectively.

Conclusion: The TI has shown a significant increase during the last time period compared to the 2 first time periods. The TI could be used as a performance indicator and be used as an incentive to promote MIS in the surgical management of endometrial cancer in gynecologic oncology.
Poster Session III

HIGH AORTO-CAVA LIMPHADENECTOMY BY TRANSPERITONEAL ROBOTIC APPROACH, USING A DOUBLE DOCKING AND 180º ROTATION OF OPERATION TABLE

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Objective: To describe and standardize the double robotic approach:

1. Upper inlet (cranial) of the arms of the Da Vinci in order to expose upper abdomen

2. Repositioning the robot to on side docking next to the right leg of the patient, to access the pelvic area.

To demonstrate the feasibility of this robotic approach in high-grade endometrial cancer or early ovarian cancer.

Methods: Since we began robotic surgery in November 2009, up to the present day, more than 35 patients have been included in this study. All of them included an upper abdominal approach to perform Aorto-Cava lymphadenectomy and then 180º rotation patient and side re-docking in order to do pelvic approach. We add a video that shows technical approach in 4 didactic steps.

Results: Median of age: 63.15 years (SD 15.00). Median BMI: 25.45 (SD 3.51).

We spend an average of 84 minutes (SD 24.20) in complete aorto-cava dissection and 17 minutes in double docking with 180º rotation of operation table.

Median of nodes extracted was 11.7 (SD 5.11) and length of hospital stay 2.2 days (SD 0.7 SD). Complications were one late lymphocele that no needed any treatment and two vena cava bleeding that requires a 5/0 Prolene suture.

Conclusions: Aorto-cava robotic lymphadenectomy is feasible and easy to do with double docking and rotation of the operation table. The learning curve is quick and secure when you have sufficient experience in cancer surgery even without having previously performed the procedure laparoscopically.
Poster Session III

VAGINAL VAULT DEHISCENCE AFTER ROBOTIC HYSTERECTOMY IN GYNECOLOGY ONCOLOGY: A RETROSPECTIVE REVIEW AND REVIEW OF THE LITERATURE

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Introduction: Vaginal vault dehiscence is a major complication following robotic-assisted hysterectomy and has been attributed to patient characteristics and surgical techniques. Our aim was to analyze risk factors in our patient population, and complement this with a literature review.

Methods: We analyzed all robotic surgeries at Jewish General Hospital, in Montreal, Canada between 19 December 2007 and 16 March 2012, and extracted data for patients with vaginal vault dehiscence following robotic-assisted hysterectomy for gynecologic oncology indications. The PubMed literature was reviewed for articles relevant to “gynecologic oncology” and “robotics” with “vaginal cuff dehiscence” in the English and French languages. Respective authors were contacted to obtain missing information.

Results: We identified 8 dehiscences at our institution out of 461 cases. The closures in these 8 were performed using interrupted 1-Vicryl (4 dehiscences out of 173), combination of interrupted 1-Vicryl and 1-Biosyn (3 out of 163), and V-lock (1 out of 125). Associated risk factors included low BMI (mean=22), adjuvant chemotherapy and/or radiation, and early resumption of sexual activity. Dehiscences occurred regardless of suturing by staff or trainees. Review of operative videos did not reveal a specific etiologic factor, such as excessive cautery damage to the vaginal cuff. Risk factors from the 38 papers identified in the medical literature included low BMI, post-operative treatment, and post-coitus triggers. Dehiscences were reported with both interrupted Vicryl and continuous V-lock sutures, but were more common with interrupted Vicryl sutures.

Conclusions: Post-operative chemotherapy and radiotherapy, and early resumption of sexual activities are risk factors for vaginal vault dehiscence. Surgical technique, particularly the use of interrupted Vicryl sutures alone deserves further evaluation.
Poster Session III

LAPAROSCOPIC RESTAGING SURGERY FOR GYNECOLOGIC MALIGNANCY

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Patients with incompletely staged gynecologic malignancies faced a new laparotomy to perform complete staging or potential under or overtreatment. Staging by laparoscopy compared with laparotomy decreased morbidity, shortened hospital stays, less post operative adhesion formations and equivalent assessment of lymph node status.

Objective: This study aimed to evaluate the feasibility and safety of laparoscopic restaging surgery in patients with incompletely staged gynecologic cancers.

Method: We performed 16 laparoscopic restaging surgery after initial surgery for an ovarian carcinoma in 7 patients, 5 endometrial cancer, 2 borderline ovarian tumors, one fallopian tube cancer and one for cervical cancer.

Results: Patients mean age was 41 years (range 16-70). The mean body mass index was 27 (range 21-40). Operative room time averaged was 241 min (145 - 300), estimated blood loss 130 ml and hospital stay 2.4 days. All except one procedures were successfully completed via the laparoscopic approach. There were one bowel injury and one laparoconversion for adhesion. We performed pelvic lymphadenectomy in 11 patients, para aortic lymphadenectomy in 12, omentectomy in 10 patients and 2 appendectomies. The pathological examination was negative for metastasis disease in all patients.

Conclusions: Laparoscopy seems to be an acceptable technical option to perform restaging of gynecologic malignancies in selected patients. Decreasing hospital stay, post operative pain and blood loss. Laparotomy for adhesions, eventual metastatic disease and risk of visceral injury may be anticipated.
Poster Session III

A PROSPECTIVE OBSERVATIONAL STUDY OF SUPRAPUBIC CATHETERIZATION VERSUS TRANSURETHRAL CATHETERIZATION FOLLOWING RADICAL HYSTERECTOMY

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The primary objectives of the study are to investigate compare prospectively the incidence of urinary tract infection (UTI), duration of hospital stay and the number of days until return to adequate voiding in women with suprapubic catheters (SPC) or transurethral catheters (TUC) after radical abdominal hysterectomy (RAH) for early stage cervical cancer.

77 patients who underwent RAH for stage IA, 1B, and 2A cancer of the cervix in University Malaya Medical Center between 1st December 2008 and 31st August 2010 were included in the study. Four gynaec-oncologists performed the surgeries. Operative, postoperative, and demographic data were extracted from patient records. Patients were catheterized either suprapubically (SPC group) or transurethrally (TUC group) according to the surgeon’s discretion. Comparative tests and multivariate regression analysis were used to compare outcome measures between the groups and to adjust for confounding variables.

The TUC group had a higher proportion of patients with UTI (42.9%) than the SPC group (10.7%) ($p < 0.001$) and postoperative hospital stay (8 vs. 7 days; $p < 0.001$). There was no significant difference in the median time return to normal voiding.

Following regression analysis, the TUC group was statistically significant in association with incidence of UTI and length of hospital stay.

The study shows that after RAH for early stage cervical cancer, SPC is statistically significant in association with a lower rate of UTI ($p < 0.001$) and shorter hospital stay ($p < 0.001$) but SPC is not statistically significant in association with the median time return to normal voiding.
Poster Session III

SENTINEL LYMPH NODE MAPPING IN ENDOMETRIAL CANCER

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Endometrial cancer has good prognosis in general, only women over age of 70 are treatment problem. These women have mostly unfavorable histopathological types and mortality is in this group over 30%. Radical surgery (pelvic and supravaginal lymphadenectomy) is morbid procedure and sentinel lymph node (SLN) identification would solve this problem. 141 women were enrolled into study, 10 was excluded (extrauterine spread, other than endometroid type). Three type of administration of radiocolloid ⁹⁹Tc and/or blue dye were compared: hysteroscopic, subserous peritumoral and subserous from 8 sites.

In 22 women hysteroscopic injection of ⁹⁹Tc was used, detection rate (DR) was 45.5%. Subserous injection of ⁹⁹Tc and blue dye was used in 66 women and DR was 72.7%. ⁹⁹Tc and blue dye were applied from 8 sites subserously in 43 patients. DR was in this group 76.7%. There were 5.34% positive lymph nodes, SLNs were positive in 4 cases, in 2 cases SLNs were false negative and in one women we didn’t detect SLNs. We identified SLN in external iliac area in 63.4%, in obturator area in 17.8%, in common iliac area in 8.9%, in parametrium in 4.3%, in presacral area in 3.3%, in low paraaortal area in 3.3%. We didn’t find any SLN above inferior mesenteric artery.

The highest DR was in group of 8 subserous injection of ⁹⁹Tc with blue dye - 76.7%, but it is still low for incorporation SLN mapping into the standard of care. Identification of SLN in endometrial cancer will still remain within experimental protocols and studies.
Poster Session III

THE AVAILABILITY OF CLOSED SUCTION DRAINAGE THROUGH THE VAGINAL STUMP AFTER SINGLE PORT ACCESS LAPAROSCOPIC ASSISTED VAGINAL HYSTERECTOMY

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Objective: To assess the feasibility and methodology for the vaginal stump drainage after single port access laparoscopic assisted vaginal hysterectomy (SPA-LAVH) and To estimate whether closed-suction drainage of the vaginal stump reduces the immediate postoperative morbidity associated with complicated SPA-LAVH.

Intervention: A total 151 women who underwent SPA-LAVH between April 2010 and February 2012. Closed-suction drains inserted through the vaginal stump into the peritoneal cavity after complicated SPA-LAVH. All cases were performed by a single surgeon (H-J Roh).

Results: For group 1 (55 women), drains were inserted through the stump into the peritoneal cavity, whereas for group 2 (96 women), no drains were placed. No statistically significant differences were seen between groups in demographics except preoperative measurements of median uterine size by sonogram (11.5 vs 9.8 cm; p=0.010). With regard to surgical outcomes, median pathologic weight (265 vs 196gm; p=0.002), operation time (80 vs 71 min; p=0.001), estimated blood loss (180.0 vs 110 ml; p=0.001) and hemoglobin change (1.5 vs 1.1 g/dL; p=0.010) were larger in the drain group than in those who had no drains. However, with respect to postoperative outcomes, there were no differences in the need for blood transfusion, hospital stay, the rate of complication, the incidence of febrile morbidity, and complications between groups.
[vaginal JP after SPA-LAVH]
### Table 1: Comparison of the preoperative characteristics in 155 patients undergoing single-port access (SPA) Laparoscopic assisted vaginal hysterectomy (LAVH)*

<table>
<thead>
<tr>
<th>Preoperative characteristic</th>
<th>Vaginal [n=107]</th>
<th>No Vaginal [n=48]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27.5 (20.75)</td>
<td>28.0 (20.75)</td>
<td>0.657</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>34.8 (6.82-13.4)</td>
<td>23.0 (6.82-13.4)</td>
<td>0.000</td>
</tr>
<tr>
<td>parity (a)</td>
<td>2 (0-3)</td>
<td>1 (0-3)</td>
<td>0.605</td>
</tr>
<tr>
<td>History of previous abdominal surgery (a)</td>
<td>15 (84.7)</td>
<td>10 (83.3)</td>
<td>0.360</td>
</tr>
<tr>
<td>Number of previous abdominal surgeries (a)</td>
<td>0 (0-3)</td>
<td>1 (0-3)</td>
<td>0.013</td>
</tr>
<tr>
<td>Overall size – long diameter (cm)</td>
<td>1.2 (1.1-1.4)</td>
<td>1.1 (1.1-1.3)</td>
<td>0.116</td>
</tr>
<tr>
<td>Preoperative diagnosis (a)</td>
<td>31 (32.7%)</td>
<td>35 (37.5%)</td>
<td>0.543</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>11 (11.3%)</td>
<td>13 (13.8%)</td>
<td>0.116</td>
</tr>
<tr>
<td>Endometrial hyperplasia</td>
<td>3 (3.3%)</td>
<td>3 (3.5%)</td>
<td>0.893</td>
</tr>
<tr>
<td>Macrometastatic cervical cancer</td>
<td>1 (1.2%)</td>
<td>2 (2.2%)</td>
<td>0.116</td>
</tr>
</tbody>
</table>

*Values are given as median(srange) or number (percentage)

### Table 2: Comparison of surgical data in 155 patients undergoing single-port access (SPA) Laparoscopic assisted vaginal hysterectomy (LAVH)*

<table>
<thead>
<tr>
<th>Surgical data</th>
<th>Vaginal [n=107]</th>
<th>No Vaginal [n=48]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical site of incision</td>
<td>35 (32.7%)</td>
<td>42 (66.5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Operative procedure (a)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hysterectomy only</td>
<td>37 (34.5%)</td>
<td>65 (66.5%)</td>
<td>0.472</td>
</tr>
<tr>
<td>Hysterectomy + BSO</td>
<td>10 (9.3%)</td>
<td>25 (52.1%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hysterectomy + LSO</td>
<td>7 (6.5%)</td>
<td>6 (12.5%)</td>
<td>0.196</td>
</tr>
<tr>
<td>Hysterectomy + IVC</td>
<td>1 (0.9%)</td>
<td>0 (0.0%)</td>
<td>0.687</td>
</tr>
<tr>
<td>Other procedures</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0.261</td>
</tr>
<tr>
<td>Size of uterus (cm³)</td>
<td>52 (24-104)</td>
<td>110 (20-238)</td>
<td>0.001</td>
</tr>
<tr>
<td>Operative time - start time (minutes)</td>
<td>40 (25-125)</td>
<td>73 (35-135)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Values are given as median (range) or number (percentage)

**BSo bilateral salpingoophorectomy, **LSo unilateral salpingoophorectomy, **IVO bilateral ovary cystectomy, **NS Not significant
Conclusions: Although the routine use of vaginal stump drains for SPA-LAVH may not be necessary, this unique drain method may be its role in SPA-LAVH in selected women, such as in those with persistent ooze from raw surfaces due to complicated surgery.
Poster Session III

ROBOTIC SURGERY EXPERIENCE IN GYNECOLOGICAL CASES: WHAT IT MEANS FOR WOMEN

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Purpose: Our aim in this study was to determine women’s thoughts on being operated on with robotic surgery and the post-surgical recovery.

Methods: This study was performed a qualitative study design. We interviewed 9 women. The women were interviewed by telephone. The interviews lasted approximately 15-20 minutes. The study is still continuing. We present the preliminary interview results of 9 women here.

Colaizzi's phenomenological analysis method was used to evaluate the data.

Results: All the women indicated having had concerns and feeling anxiety while making the decision for robotic surgery due to the novelty of the procedure and not having heard of it before. Three women indicated having had concerns that the surgeon’s hands might slip, that he/she might not be able to control the buttons, and that an incorrect procedure might take place during the operation. However, all the women indicated that the confidence they had in their surgeons alleviated their concerns and influenced their decision to accept undergoing robotic surgery.

Six of the women indicated they had no symptoms during the recovery period following robotic surgery, and that they did not feel they needed assistance. However three women indicated they had suffered severe leg pain, distension, groin pain and vaginal dryness postoperatively.

Conclusion: The women in this study indicated that they had concerns as this is a new procedure, but their decision was influenced by the confidence they had in their doctors.
Poster Session III

OPTIMAL CYTOREDUCTION WITH NEUTRAL ARGON PLASMA ENERGY IN SELECTED OVARIAN AND PRIMITIVE PERITONEAL CANCER PATIENTS

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Introduction: Epithelial ovarian cancer (EOC) is a deadly disease for which optimal cytoreduction to microscopic disease has shown the best correlation for survival. Neutral argon plasma technology is a novel alternative to allow aggressive cytoreduction in selected EOC, primary peritoneal and tubal cancer.

Methods: This is a prospective feasibility study using neutral argon plasma technology to complete staging surgery and report on its ability to obtain optimal cytoreduction.

Results: Six patients had their surgery completed with the neutral argon plasma devise. None of the patients would have had optimal surgery unless the device had been available. All patients were cytoreduced to less than 5-10 mm without additional morbidity.

Conclusion: Neutral plasma argon technology is a useful technology to allow further cytoreduction and to reduce tumor burden in selected cases of EOC.
Poster Session III

SURGICAL TREATMENT OF INTRAVENOUS LEIOMYOMATOSIS WITH INTRACAVAL AND INTRACARDIAC EXTENSION

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Objective: To report the results of management of intravenous leiomyomatosis (IVL) with intracaval and intracardiac extension in Peking Union Medical College hospital.

Methods: We review a cohort of twenty patients with surgically and histopathologically proven IVL extending to the inferior vena cava (IVC) and heart focusing on the results of surgical management and prognosis.

Results: The mean age of the patients was 43.3±5.5 years. All the patients had history of uterine leiomyoma and 17 patients (85%) had undergone an operation of uterine leiomyoma. After careful preoperative evaluation including CTA, CTU, MRI, venography, echocardiography and slides review, and according to the condition of intracardiac extension, 8 patients underwent one-stage operations (cardiac surgery + vascular and gynecological surgery together); and 12 patients underwent two-stage operations (cardiac surgery first, then vascular and gynecological surgery). The mean blood loss in one-stage operations was 5488 ml, however in two-stage operations 3225ml (p< 0.05) There was no significant difference in the postoperative complication rate and hospitalization between one-stage and two-stage operation (37.5% vs. 27.3%, p=1.000). All operations were successfully performed. 75% of patients had complete tumor resection and 25% of the patients experienced incomplete resection. 15 (60%) patients received hormone therapy postoperatively. During mean follow up time of 23.3 months, recurrence occurred in 5 patients (25%), but all the patients were survived.

Conclusions: IVL with intracaval and intracardiac extension can be removed with either one-stage operation or two-stage operation. Precise and full-scale preoperative evaluation, complete tumor resection and multi-disciplinary cooperation are very important for successful treatment.
Poster Session III

MINIMALLY INVASIVE SURGERY FOR ENDOMETRIAL CANCER: DOES SURGICAL START TIME IMPACT OPERATIVE OUTCOMES?

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Objective: The objective of this study was to examine the effects of operative start time on surgical outcomes for patients undergoing laparoscopic surgery for endometrial cancer.

Methods: A retrospective review was conducted of patients undergoing laparoscopic surgery for endometrial cancer at a single institution between 2000 and 2011. Operative start time, beginning before or after noon, was the independent variable of interest.

Results: A total of 173 patients were included in the study (39 with start times after noon and 134 with start times before noon). There was no difference in number of prior surgeries, medical comorbidities or BMI between the two groups. No significant differences were observed for intraoperative complications (5.1% of patients after noon vs. 4.5% of patients before noon, \( p=0.999 \)), estimated blood loss (median 100 cc vs. 100 cc, \( p=0.507 \)), blood transfusion rates (7.7% vs. 9.7%, \( p=0.999 \)), conversion rates to laparotomy (7.7% vs. 9.0%, \( p=0.999 \)), or percent of patients who underwent lymphadenectomy (\( p=0.335 \)). Additionally, no differences were found with respect to tumor grade (\( p=0.889 \)), histology (\( p=0.880 \)), or stage (\( p=0.976 \)). There was no association between operative start time and postoperative non-infectious complications (15.4% vs. 16.4%, \( p=0.999 \)), postoperative infections (25.6% vs. 21.6%, \( p=0.493 \)), or length of hospital stay (median 2 days vs. 2 days, \( p=0.594 \)). However, the median operative time was shown to be longer for cases beginning before noon (241 minutes vs. 199 minutes, \( p=0.039 \)).

Conclusion: Our results indicate that surgical outcomes do not differ significantly based on operative start time. However, surgeries begun before noon took longer.
Poster Session III

FEASIBILITY AND CLINICAL VALUE OF MODIFIED ELECTROSURGICAL KNIFE CONIZATION

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Objective: To evaluate the feasibility and clinical value of a modified electrosurgical knife conization (EKC) procedure.

Methods: Two hundred and ten patients received EKC in Gynecological Cancer Center in Peking Union Medical College Hospital between November 2010 and October 2011. Modified steps mainly included local injecting normal saline added with norepinephrine in cervix, setting an appropriate electrosurgical knife power, speeding up the excision procedure and no coagulating the specimen side. Iodoform gauze was placed into the cervical canal after the remodeling and ulcers oil gauze were stuffed into the vagina for helping hemostasis. 180 case of standard cold knife conization (CKC) performed during the same interval were collected as control.

Results:

1. Pathologic examination showed no obvious marginal destroy occurred in EKC in compared with CKC;

2. Operating time for EKC and CKC was 24.7±9.2 min and 29.2±11.6 min respectively (P< 0.01), blood loss during operation for EKC and CKC was 13.1±8.2 ml and 25.5±14.2 ml respectively (P< 0.01);

3. The thickness of conization in EKC and in CKC was 19.7±5.1 mm and 19.3±4.8 mm respectively (P>0.05), and 12 cases (5.7%) of conization sample in EKC and 10 cases (5.5%) in CKC had positive endocervical margin (P>0.05).

4. One patient (0.5%) in EKC group and 4 patients (2.2%) in CKC group occurred postoperative cone-bed bleeding.

Conclusions: With modification of the procedure, EKC is an valuable alternative conization method which obtains equivalent excision effects to CKC and does not affect the integrality of margin, while owns shorter operating time, less bleeding and reduced morbidity.
Poster Session III

UTILIZING A NEW DOUBLE LAYER VAGINAL CUFF CLOSURE TECHNIQUE AFTER TOTAL LAPAROSCOPIC HYSTERECTOMY, AND THE INCIDENCE OF VAGINAL CUFF DEHISCENCE

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Background/purpose: Multiple techniques are described in the literature to close the vaginal cuff after total laparoscopic hysterectomy (TLH). The aim of this study is to evaluate the incidence of vaginal cuff dehiscence utilizing a new double layer vaginal cuff closure technique.

Methods: A retrospective review was conducted on all women who underwent TLH and had the vaginal cuff closed with the Endo Stitch™ suturing device. All procedures were performed by the surgeons at The Women’s Cancer Center of Nevada from 1996-2011. Technique: Grasping the vaginal cuff posteriorly in the midline with a Maryland grasper, the Endo Stitch™ with 0 Polysorb™ anchored the first suture, using a loop fashioned at 25 cm. from the needle. Using a running vertical mattress technique, the suture is advanced anteriorly to include approximately 1.5 centimeters of tissue on both edges. Once the anterior vaginal apex was reached, the second layer, using a similar technique, was initiated, beginning at the anterior vaginal apex and ending at the posterior vaginal apex, near the anchoring stitch.

Results: Out of 252 patients identified, 1 had a vaginal cuff dehiscence. The rate of vaginal cuff dehiscence was 0.40%.

Conclusion: As compared to the current literature, the vaginal cuff dehiscence incidence in this study, using a new double layer closure technique with the Endo Stich™, is at least 40% lower than reported dehiscence rates (0.7- 1.2%). We conclude that the double layer vaginal cuff closure technique should be adopted by surgeons who perform TLH as the preferred closure method.
Poster Session III

MEDIUM TO LONG TERM MORBIDITY AND OUTCOMES AFTER ROBOTIC SURGERY FOR ENDOMETRIAL CANCER

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Objective: Although intra-operative and immediate postoperative complications of robotic surgery are relatively low, little is known about following medium to long-term morbidity. Our goal was to assess both short- and medium term morbidities after robotic surgery for comprehensive endometrial cancer staging.

Methods: Patients who underwent robotic staging for endometrial cancer between 2008 and 2011 were identified. The period 2008-2009 was considered as the learning curve time and 2010-2011 as post-learning curve. All patient’s charts were retrospectively analysed for surgical complications and postoperative morbidities.

Results: 107 patients were identified. In 2008-2009 median BMI was 27.5 (range 23-36) and in 2010-2011 median BMI was 30 (range 21-44) (p=0.03). There was overall rate of 24.7 pelvic and paraaortic lymphnodes. Pelvic lymphadenectomy with extrafascial hysterectomy was performed in all patients. Additionally in 21% of patients the aortocaval lymphadenectomy was performed for high risk preoperative assessment.

4 cases (3.7%) were converted to laparotomy. No cystotomies, no ureteric injury, no enterotomies, and no vessel injuries occurred (0% intra-operative complications). 3 (2.8%) patients developed major postoperative complications. 1 patients (1%) required a transfusion in the 48-hours peri-operative period. There was no venous thromboembolism (VTE). No partial or complete cuff dehiscence was observed. No case of lymphedema occured.

Conclusions: This study provides a cohort of patients with robotic-assisted hysterectomy and lymphadenectomy with an assessment of morbidity. As demonstrated, robotic surgical staging can be safely performed with a low risk of short-, medium and long-term complications.
Poster Session III

STANDARDIZED TRANSPERITONEAL LAPAROSCOPIC LYMPHADENECTOMY FOR GYNECOLOGIC MALIGNANCIES IN A BRAZILIAN CANCER CENTER, INITIAL EXPERIENCE


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Introduction: In order to reduce complications and achieve oncological goals with safety, it is important to standardize surgical procedures.

Objective: To report the initial experience with standardized laparoscopic lymphadenectomy in a gynecologic oncologic Brazilian cancer center.

Methods: Surgical data from all patients were prospectively recorded (November/2010 to January/2012). Patients were positioned in a low lithotomy position, over a foam cushion, with arms tucked along the trunk and lower limbs in Allen stirrups. One 11mm trocar was placed in the umbilical site, and three 5mm were positioned in the hypogastrium, left and right lower quadrants. Transperitoneal exposition of the paraortic and pelvic spaces was achieved. Paraortic removal of lymphovascular tissues was extended up to the left renal vein. Most patients underwent hysterectomy at the same procedure. Data regarding age, body mass index (BMI), surgical time, blood loss, complications, lymph nodes retrieved were analyzed.

Results: In a total of 85 patients, mean age=50.7yo. Obese patients were 58.8% (50/84). Mean surgical time was 242 minutes. Radical hysterectomy (Type B or C1) was performed in 26 patients, pelvic lymphadectomy in 51, paraortic in 5, and both in 29. Median blood loss was 80ml. Mean number of pelvic lymph nodes was 19 and 15.4 paraortic. Operative injuries occurred in 10 cases: vascular (n=8), urinary tract (n=1), and bowel (n=1). Laparotomy was necessary in 4 patients, due to specimen extraction (n=2), adequate nodal debulking (n=1), and vascular injury (n=1). One patient received transfusion (2UI). Conclusion: This initial experience with standardized laparoscopic lymphadenectomy revealed acceptable surgical outcomes.
Poster Session III

BILATERAL SALPINGOOHORECTOMY FOR OVARIAN ABLATION IN PATIENTS WITH ADVANCED BREAST CANCER PERFORMED BY SURGICAL RESIDENTS


Barretos Cancer Hospital, Barretos, Brazil

Background: Bilateral laparoscopic oophorectomy is an effective and feasible alternative for ovarian ablation in women with locally advanced or metastatic breast cancer. As a low risk procedure, it seems to be a good option to start a laparoscopic practice.

Aim: To report the experience with this technique, performed by residents under close assistance, in a referral Brazilian cancer center.

Methods: Data from all cases between December/2010 and October/2012 were prospectively collected. Patients were submitted to conventional laparoscopy by means of one 11mm (umbilicus) and two or three 5mm trocars. Residents in their third to fifth years of training were allowed to perform the surgery, under assistance and/or close guidance of an experienced surgeon.

Results: 25 patients were submitted to bilateral salpingoophorectomy in this setting. Mean age was 42yo. Mean body mass index was 27, including 76% (19) obese patients. Mean surgical time was 62minutes. One vascular injury demanded external iliac artery suture. There was no need of blood transfusion. All patients were discharged in 12 to 24 hours after surgery.

Conclusion: Minimally invasive techniques for ovarian ablation seems to be a good option for teaching laparoscopy, with low morbidity and acceptable surgical time. Further studies are in need to address the validation of the technique and the learning model.
Poster Session III

AN UNUSUAL CASE WITH MULTIPLE RETROPERITONEAL VASCULAR ANOMALIES

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Background: Anomalies of major retroperitoneal vascular structures have been presented with a prevalence of 13.6%-30.2%. They are mostly diagnosed either during surgery or by imaging techniques.

Case report: We report a group of vascular anomalies of retroperitoneum which were encountered during the staging surgery of 65 years-old woman with endometrium carcinoma. The findings were:

1. A ptotic right kidney.
2. There were three right renal arteries.
3. One of the arteries supplying the right kidney was a branch of an artery originating from abdominal aorta at a level below inferior mesenteric artery and giving branches two both kidneys by ascending upwards.
4. One artery supplying the right kidney was originating from the right common iliac artery.
5. Right ovarian vein was a tributary of right renal vein.
6. There were two renal veins on the right side.
7. All three renal arteries on the right side were overpassing the inferior vena cava (precaval renal arteries).
8. There was no abnormality in the left side except the unusual course of the left renal artery, supplying the left kidney by ascending upwards after originating from a common renal artery stem.

There was no vascular injury during the surgery associated with these vascular abnormalities.

Conclusion: Since they are met quite frequently, it is important for surgeons dealing with retroperitoneum to be aware of the possible anomalies of vascular and renal structures in this region.
Poster Session III

ASSESSMENT OF EPITHELIAL DENUDATION OF CERVICAL CONIZATION SPECIMEN

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Objectives: We evaluated whether epithelial denudation contribute to prognosis and diagnosis in cervical conization specimen.

Methods: The medical records of 138 patients with cervical intraepithelial neoplasm who underwent conization surgery with ultrasonic scalpel at Osaka General Medical Center between January 2007 and December 2011 were reviewed. We analyzed prognosis of the positive margin cases and the cases of epithelial denudation.

Results: In final diagnosis, patients of CIS, severe dysplasia and moderate dysplasia are 74, 52, and 12, respectively. In assessments of margin, positive and negative are 7 cases (5%) and 104 cases (75.3%), respectively. We could not make assessment of margins of 27 cases (19.5%) because of epithelial denudation or coagulation artifact. Fifty-three cases (38.4%) showed epithelial denudation or coagulation artifact that made recognition of histological diagnosis extremely difficult or impossible (unsatisfactory cases). Cases of epithelial denudation and cases of coagulation artifact were 46 (33.3%) and 4 (3%), respectively. Recurrence is defined as lesion speculated CIN 1 or more by cervical cytology. The recurrence were diagnosed in sixteen cases. The cases of positive margin showed higher rate of recurrence than the cases of negative margin; 2/7 and 10/104 respectively. The recurrence rate of satisfactory cases and unsatisfactory cases did not differ (p>0.5).

Conclusion: Evaluation of the conization specimens revealed relatively high rate of inadequate epithelial condition for appropriate evaluation. Careful follow up should be undertaken for such cases.
ABDOMINAL RADICAL TRACHELECTOMY: AN INTERNATIONAL SERIES OF 199 CASES

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Objectives: Abdominal radical trachelectomy (ART) is a type C resection in which the uterine vessels are ligated at their origin from the hypogastric. As a result of the interruption in vasculature, some question whether fertility is maintained. Additionally, ART inclusion criteria are expanded to larger tumors when compared to vaginal radical trachelectomy (VRT), raising concerns regarding survival outcomes. We report an international series on ART to describe fertility and oncologic outcomes.

Methods: Databases at 4 institutions were queried to identify patients planned for ART from 1999-2011. Clinical and demographic data were gathered.

Results: One hundred ninety-nine patients underwent attempt at ART. Mean age was 31 years (range, 19-44). Histology was adenocarcinoma (n=65), squamous (n=123), adenosquamous (n=10), and clear cell (n=1). One hundred sixty-six (83%) underwent trachelectomy, while 33 (17%) required hysterectomy. The indications for hysterectomy were: nodal metastasis (n=12), margins (n=14), recurrence (n=2), and patient choice (n=5). Postoperatively, 35 (18%) patients received adjuvant chemotherapy and/or radiation (22 nodes, 5 margins, 8 other). Five patients (2.5%) recurred and are living 9-35 months after diagnosis (3 currently without evidence of disease). Of the 147 women who had neither hysterectomy nor adjuvant therapy, 55 (37%) attempted pregnancy and 32 (86%) achieved pregnancy. Thirty-five pregnancies resulted in 17 (49%) third-trimester deliveries.

Conclusions: These data demonstrate that both oncologic and fertility outcomes are maintained with ART. Thus, preservation of the uterine vasculature is not mandatory for fertility and the expanded inclusion criteria do not appear to result in poor survival outcomes. Gynecologic oncologists should consider offering ART to eligible patients.
Poster Session III

LEARNING CURVE FOR LAPAROSCOPIC RADICAL HYSTERECTOMY FOR CERVIX CANCER: A SINGLE-OPERATOR EXPERIENCE

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Background: Laparoscopic radical hysterectomy for cervix cancer is increasingly being performed worldwide. This study aimed to evaluate the learning curve for laparoscopic resection for cervix cancer of one gynecologic oncology operator. The purpose of present study is to evaluate factors related to the learning curve of laparoscopic radical surgery, such as the number of operations performed, operation time, major complications, and oncologic resections.

Methods: Data were analyzed for 128 consecutive patients who underwent laparoscopic radical hysterectomy for cervical cancer between March 2004 and April 2012. Surgery was performed by a single operator. The learning effect was evaluated by review of medical records retrospectively. Surgical outcomes and operation parameters were evaluated.

Results: The mean age of the study population was 52 years and mean operative time was 238 minutes. Operating time for laparoscopic radical hysterectomy for cervical cancer reached a steady state after 25 cases. Significant surgical complications occurred in 4 patients that included vessel injury. There was a significant decrease in complications after the first 40 laparoscopic radical hysterectomy. The mean number of lymph node harvested during operation was 46. Hospital stay averaged 13 days.

Conclusions: The present study shows that laparoscopic radical hysterectomy for cervical cancer may be achieved early in the learning curve. Laparoscopic radical hysterectomy is not difficult to perform and recommended as a treatment for cervical cancer.
Poster Session III

CLINICAL RESEARCH OF OLANZAPINE FOR PREVENTION OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING RESISTANT TO STANDARD ANTIEMETIC THERAPY FOR HIGHLY EMETOGENIC CHEMOTHERAPY

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Background and aims: Olanzapine is an antipsychotic which blocks multiple neurotransmitters in the central nervous system and has antiemetic activity for chemotherapy-induced nausea and vomiting (CINV). The purpose of this retrospective study was to assess the effectiveness of olanzapine for the prevention of CINV in patients with severe emesis regardless of standard antiemetic therapy for highly emetogenic chemotherapy (HEC).

Methods: Olanzapine was administered in seventeen gynecological cancer patients who received chemotherapy with the combined use of palonosetron, aprepitant and dexamethasone and had grade 3 nausea (CTCAE ver.4.0) for the overall period (0-120 hours postchemotherapy). Oral olanzapine (5 mg/day) was administered on day -1 prior to chemotherapy and continued for 7 days.

Results: The average grade of nausea decreased from 3 to 0.94±0.9 for the overall period, 1.94±1.03 to 0.41±0.87 for the acute period (24 hours postchemotherapy), and 2.88±0.33 to 0.88±0.86 for the delayed period (days 2-5 postchemotherapy). In all period, the average grade of nausea decreased significantly (p < 0.005). Thirteen patients (76%) was controlled in grade 0~1. Complete response was 35% despite of uncontrolled patients with standard antiemetic agents. The adverse events were only grade 1-2 somnolence in eight patients. There were no grade 3 or 4 toxicities.

Conclusion: Olanzapine could improve the degree of CINV in most of patients with grade 3 emesis regardless of the standard antiemetic therapy. In this study, the use of olanzapine for chemotherapy-naive patient demonstrated additional improvement in the control of acute and delayed CINV.
**Poster Session III**

**IMPROVING SURVIVORSHIP FROM PELVIC RADIATION DAMAGE IN PATIENTS WITH GYNAECOLOGICAL CANCERS - SINGLE CENTRE EXPERIENCE**

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**Aim:** A retrospective study to identify how many patients had developed new and/or persistent changes in their bladder and bowel habits after pelvic radiotherapy/brachytherapy.

**Method:** A questionnaire was developed and sent to 109 patients who had completed pelvic radiotherapy to identify late changes in bowel/bladder function unknown to their cancer specialists. Level 3-5 was severe symptoms.

**Results:** 71% (77/109) of patients sent the questionnaire responded. Of the 84% (65/77) of patients who had experienced changes in their bowel and/or bladder function, this varied from mild to more severe effects (e.g. opening bowels more than ten times in 24 hours). The frequency of patients suffering level 3-5 bowel symptoms was as follows: change in bowel habit 82% (63/77); pain/discomfort 77% (59/77); diarrhoea 60% (46/77); faecal incontinence 51% (39/77); mucus, sticky or slimy faeces 44% (34/77); rectal bleeding 8% (6/77). One patient has been treated for malabsorption. The frequency of level 3-5 bladder symptoms was as follows: urgency 84% (65/77); pain on micturition 78% (60/77); incontinence 50% (39/77) (5/39 wearing pads); recurrent infection 32% (25/77); haematuria 25% (19/77). Four patients had stomas.

**Conclusion:** This study recognizes that there is a significant number of patients suffering from late bladder and/or bowel toxicity which is under reported. The above results have led us to improve our service in pelvic radiation damage management by using a multi-disciplinary team approach. This study highlights the need to adopt a more focused approach on improving the quality of life and survivorship of patients cured from gynaecological cancers.
Poster Session III

ROLE OF EXTERNAL BEAM RADIATION THERAPY (XRT) FOR PALLIATION IN HEAVILY PRETREATED RECURRENT OVARIAN CANCER

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Background: To investigate the role of XRT in the treatment and palliation of recurrent ovarian cancer.

Methods: A total of 30 patients (pts) with heavily pretreated recurrent ovarian, primary peritoneal, or fallopian tube cancer who received XRT were identified in this IRB approved retrospective single institution study.

Results: The study population had a median OS of 18.8 m and PFS of 10.4 m. Most patients received pelvic XRT with a median dose of 45Gy (range 15-70.2). 79% of patients were platinum resistant. The median number of prior lines of chemotherapy was 3 (range 1-6). Radiation was well tolerated with few complications: 7 pts had grade 2 radiation enteritis, 2 pts had grade 2 radiation cystitis, 1 case of sacral insufficiency fracture, and 1 case of grade 3 lymphedema. 74% were treated with a full prescribed dose of XRT that was at least 40Gy. The PFS and OS were significantly longer in those pts treated with greater than 40Gy at 11.6 m compared to 1.2 m and 22.8 m compared to 1.2m respectively. For comparison, a meta analysis of 10 phase 2 co-operative group chemotherapy trials for recurrent platinum resistant disease showed a median PFS of 3.3 m and median OS of 10 m.

Conclusions: Our study shows that using XRT in select patients with recurrent ovarian cancer is well tolerated and can be an effective modality for palliation yielding lasting results that are comparable if not superior to prospective phase II chemotherapy trials.
Poster Session III

PRESERVATION OF OVARIAN FUNCTION AND QUALITY OF LIFE (QOL) IMPACT AFTER RADIOTHERAPY TREATMENT

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Purpose: To investigate the role of function ovarian preservation by ovarian transposition and after laparoscopic ovarian excision with ovarian cryopreservation tissue, prior to radiotherapy (brachytherapy (BRT), 3Dconformal radiotherapy (3DCRT), intensity modulated radiotherapy with rapidarc (RA-IMRT).

Material and methods: From February 2008 to April 2011, 4 pts underwent preservation of ovarian function by ovarian transposition before radiotherapy or chemoradiation. The mean age was 29 years (range 17-36). The classification of disease was: right inguinal fibroblastoma (one pt), inguinal skin epithelioid sarcoma (one pt), vaginal carcinoma with cervix infiltration (2 pts), respectively. The first pt received surgery plus adjuvant 3DCRT (59.4 Gy) in inguinal right area, the second pt received surgery and interstitial high dose rate (HDR) BRT (34 Gy), 2 pts received radiotherapy (IMRT-RA 45 Gy plus pulsate dose rate (PDR) BRT 30 Gy) and concomitant chemoradiotherapy (IMRT-RA 50 Gy plus BRT 25 Gy with concomitant CDDP plus PTX), respectively.

Results: All pts are alive in complete remission of disease. The first pt, after 3 year follow-up, is experiencing normal menstrual cycles at regular monthly intervals. For the other pts the follow-up is shorter but the pts that received IMRT-RA had normal menstrual cycle during the treatment.

Conclusions: Ovarian transposition is a simple surgical procedure that can be used in order to reduce the risk of early menopause in young patients. The introduction of new radiotherapy techniques like IMRT-RA was useful in sparing organ at risk (OAR) and and creating a dose painting in the "risk area".
Poster Session III

RESCUE OF SUSTAINED CHEMOTHERAPY-INDUCED THROMBOCYTOPENIA WITH ORAL THROMBOPOIETIN RECEPTOR (TPO-R) AGONIST, ELTROMBOPAG, IN PATIENTS WITH GYNECOLOGIC CANCER


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Introduction: Chemotherapy-induced thrombocytopenia (CIT) is one of the most common side effects that delay chemotherapy and lower the dose intensity. The pilot study was aimed at rescuing sustained CIT with eltrombopag that had been approved by FDA on ITP.

Material and method: In Chang Gung Memorial Hospital, patients with gynecologic cancer developing CIT (< 75,000/uL) on the day scheduled for chemotherapy were put on a 7-day eltrombopag treatment, 50 mg/day, to achieve an aim of platelet count > 75,000/uL.

Results: Six patients with ovarian cancer (N=5) or endometrial cancer (N=1) were enrolled from Dec. 2011 to April 2012. The median age was 63 years (range, 55 - 72). The median line of chemotherapy was 2 (range, 1 - 3). Before eltrombopag treatment, the mean delayed days for chemotherapy was 6.7 days (range, 1 - 23 days). The median platelet count before and after treatment was 43,000/uL (range 21,000 - 64,000) and 109,500 (range 32,000 - 157,000), respectively. The platelet counts elevated to > 75,000/uL in 4 out of the 6 patients (66.7%). Five patients, including 1 whose PLT at 70,000/uL, underwent further chemotherapy after the 7-day oral eltrombopag.

Conclusion: The oral TPO-R agonist, eltrombopag, at the dose of 50 mg/day might be effective for sustained CIT for patients with gynecologic cancers. A randomized prospective trial will be done for more solid evidence.
Poster Session III

PERITONEAL CARCINOMATOSIS SIMULATING TUBERCULOSIS PERITONITIS: VALUE OF ADENOSINE DEAMINASE (ADA) IN ASCITIC FLUID

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Subject: To evaluate the usefulness of ADA in ascitic fluid as a differential diagnostic tool for peritoneal carcinomatosis (PC) VS Tuberculosis peritonitis (TP).

Methods: A retrospective review of women with PC or TP who were managed at Ilsan Paik Hospital from May 2001 to December 2010.

Results: During the study period, 23 patients were PC and 81 patients were TP. All patients had ascitic fluids. There were no between-group differences in mean age (57.9 years in PC and 42.7 years in TP, P=0.68), parity, menopausal status, nor was there between-group difference in mean CA-125 level (2413 (range 103-6320) in PC and 1650 U/ml (range, 93-3830) in TP, P= 0.89). However, the TP patients had significantly higher mean ADA levels in ascitic fluid than PC patients (108 IU/L (range 48.3-158.7) in TP and 26.8(range 8.3- 40.2 IU/L) in PC, p= 0.023).

Conclusions: Most of examinations are not sensitive enough to determine the presence of TP or to differentiated those from PC. Measurement of ADA level in ascitic fluid is a fast and accurate test for differential diagnosing PC and TP. The empirical treatment when a patient has a high ADA level seems to be a reasonable treatment and measurement of ADA level is essential who has ascitic fluids in endemic area.
Poster Session III

OVERVIEW OF PALLIATIVE CARE IN NEPAL AND THE CHALLENGES

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Background: Majority of cancer patients in Nepal are diagnosed in advanced stage but palliative care is not available in most part of the country. Barriers to palliative care are related to physicians, patients and policies. Palliative care in Nepal is still unachievable.

Methods: This is a review of existing palliative care services, policies and activities in Nepal. Data regarding cancers and palliative care were collected from different institutions and providers.

Results: Seventy percent of cancer patients in Nepal come at the late stage. Due to increase in cancer prevalence and elderly population, terminal illness is also increasing and there is an increase in the number of patients needing palliation. This study showed that the palliative care facility in Nepal is limited and grossly inadequate with few institutions providing palliative care in the capital city and none in small towns. Opioids use and availability is limited to big cities only and is under-prescribed due to fear of misuse, lack of awareness, shortage of resources and legal regulations.

Conclusions: Palliative care is a need in Nepal. Being a new specialty, palliative care is yet to be incorporated in the existing national health system and there is no national policy on palliative care. All should have access to care during a serious illness and at the end of life. It needs combined efforts to establish state of art palliative care in the country by formulating national policy, incorporating it in the medical curricula and raising awareness.
Poster Session III

IMPACT OF HEALTH RELATED QUALITY OF LIFE ISSUES AFTER GYNECOLOGIC ONCOLOGY SURGERY

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Background: Minimally invasive surgery offers patients shorter hospital stays and quicker recovery times with cosmetically appealing incisions. This study seeks to identify factors that influence patient recovery and improve health related quality of life measures.

Methods: A prospective, non-randomized cohort study was conducted. Ninety two patients underwent open or minimally invasive surgery in the department of gynecologic oncology. All patients completed the ENRICHD Social Support Instrument, Body Image Scale, and Memorial Symptoms Assessment Scale. These validated questionnaires were completed preoperatively then two weeks, six weeks, six months and twelve months postoperatively using a repeated measures design. The test for trends between surgery groups over time was done using a mixed analysis of variance model for quality of life scores as a function of the type of surgery over time.

Results: Fifty-nine percent of patients had a cancer diagnosis on final pathology and 57% percent of patients underwent minimally invasive surgery. No difference was seen in the global distress index over time in either group, however, less disturbance in body image at six weeks postoperatively was seen in all patients undergoing minimally invasive surgery (p=0.045). The subset of patients with a cancer diagnosis who underwent minimally invasive surgery experienced a sustained improvement in body image (p=0.035).

Conclusions: While modest improvements in most health related quality of life measures diminished throughout the postoperative period, cancer patients undergoing minimally invasive surgery had an improved perception of their body image that was sustained over time.
Poster Session III

SCREENING FOR DISTRESS IN AN AMBULATORY GYNECOLOGIC CLINIC

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Cancer treatment has more than a physical impact. There are emotional, psychosocial, and practical consequences as well. Unfortunately, the tumor diagnosis and treatment takes precedence and psychosocial and symptom distress can be overlooked. In busy clinical settings there ought to be concrete strategies for identifying supportive care needs and those individuals who would benefit from intervention.

The purpose of our work was to implement a programmatic strategy for screening for distress (6th vital sign) in our gynecologic clinic.

Application of the standardized self-report screening tool (Edmonton Symptom Assessment System and Canadian Problem Checklist) provided the opportunity for patients to indicate which concerns they were experiencing prior to conversation with the oncology nurse and/or physician. Based on the conversation, deeper assessment was completed for the specific issues the patient identified. Intervention and follow-up actions were based on this assessment.

A total of 2342 women attending the gynecologic cancer clinic were screened in the 6 month period of initial implementation. Thirty-one percent had at least one symptom distress score in the severe distress range and another 30% had at least one score in the moderate distress range. The most frequently identified symptoms in the sever category included feeling tired (16%), feeling of well-being (11.8), anxiety (11.5%) and appetite (9.2%).

Women experience both physical and psychosocial consequences following cancer treatment. Use of a self-report, standardized screening tool can be helpful in easily identifying the concerns women experience and providing a focus for an effective and meaningful discussion in a busy clinic setting.
THE OUTCOME OF PALLIATIVE CARE INCLUDING BOWEL SURGERY FOR MALIGNANT BOWEL OBSTRUCTION IN PATIENTS WITH GYNECOLOGIC MALIGNANCY

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Aim: To evaluate outcomes of patients with gynecologic malignancy who had palliative care including bowel surgery for malignant bowel obstruction (MBO).

Methods: Medical records of patients with MBO due to gynecologic malignancy treated at our institute between 2005 and 2010 were reviewed. Successful palliation after surgery was defined as the ability to tolerate solid food at least 60 days. Clinical variables were analysed using Chi-square or Fisher's exact test. Survival was evaluated using Kaplan-Meier method and log-rank test.

Results: Fifty-three cases were identified; 20 had surgery and 33 did not. Post operative morbidity was 35% and mortality within 30 days was 5%. Successful palliation was achieved in 14 (70%) of 20 cases with median period of 146 days (range 61-294). Survival after diagnosis of MBO was better in cases with surgery than those without (median survival time 146 versus 69 days; p< 0.0001). Although age, presence of ascites, laboratory values and types of prior anti-cancer therapy were not significantly different, longer interval from last anti-cancer therapy to diagnosis of MBO was observed in patients with surgery than those without (median 57 versus 30 days; p< 0.05) besides better performance status. Among the patients with surgery, the interval was also longer in patients with successful palliation than those without (median 83 versus 32 days; p< 0.05).

Conclusions: The palliative benefit by surgery for MBO in selected patients with gynecologic malignancy was observed. The interval from last anti-cancer therapy to diagnosis of MBO might serve as a prognostic factor when considering the surgical intervention.
Poster Session III

SEXUALITY AND SEXUAL ISSUES IN GYNECOLOGICAL CANCER

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Background: Prevailing perceptions and available data regarding sexual function in gynecological cancer patients is sparse and mostly limited to cervical cancer.

Methods: Cross-sectional study of patients with gynecologic cancers in a tertiary cancer center. Patients were asked to complete questionnaires assessing the emotional (intimacy and couple communication) and physical components of their sexuality before, during and after treatment.

Results: Only 93 of 140 questionnaires distributed were completed. The majority of subjects were aged 51-70 years and had ovarian or endometrial cancer. A significant decrease in sexual comfort, desire, frequency (manually/with partner), and orgasms was observed during treatment, which persisted after treatment. Other aspects of intimacy - including hugging, communication with partners and sensitivity to emotional well-being - were reported as not significantly affected.

The majority of patients never discussed these issues with their gynecology oncology team; however 47% would have liked the topic of sexuality to have been brought up. In terms of patient resources, the internet and doctor were cited as the most accessed sources of information on sexuality and cancer treatment.

Conclusions: Our data demonstrates persistent sexual dysfunction related to the treatment of gynecologic cancer, but appears not to extend to the realm of intimacy with partners.
Poster Session III

INTERSTITIAL IMPLANTATION OF $^{125}$I SEEDS AS SALVAGE THERAPY FOR RECURRENT OVARIAN CANCER AND CERVICAL CANCER

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Objective: To investigate the feasibility, short-term efficacy and adverse effects of $^{125}$I seeds implantation in the treatment of recurrent ovarian cancer and cervical cancer.

Methods: A total of 12 patients with recurrent ovarian cancer and 17 patients with cervical cancer treated in Sun Yat-sen University Cancer Center from June 2009 to December 2010 enrolled into the study. There were 49 lesions including 25 ovarian cancer lesions and 24 cervical ones. Forty-five lesions were treated with $^{125}$I seed implantation. Forty-four were treated under the guidance of CT while only one lesion under the guidance of ultrasonography. The treating plan was calculated using computerized treatment planning system (TPS) and Memorial Sloan-Kettering nomograph. The prescribed matched peripheral dose (MPD) was 100～160 Gy. The total number of sources implanted were 6～68 with a median number of 20.5. Additional chemotherapy was given to 13 patients. Tumor status were evaluated with CT and $^{18}$F-FDG PET/CT findings.

Results: Nineteen patients were still alive after a median follow-up of 15 mouths (range from 5 to 19mouths). Thirteen patients showed complete remission, seven patients showed partial remission. The effective rate was 69.0% (20/29). There were three patient suffered from Sciatic nerve injury symptoms. No complication was found in the other patients.

Conclusion: $^{125}$I seed implantation was feasible, effective and safe as a salvage local treatment for patients with recurrent gynecologic malignancies, it was worth of development and promotion. The efficacy seems better in recurrent ovarian cancer than in cervical cancer patients.
Poster Session III

SERVICE EVALUATION OF FOLLOW-UP CARE OF GYNAECOLOGICAL CANCER PATIENTS IN SOUTH-EAST WALES

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Background: With 2 million cancer survivors in the UK traditional methods of oncological follow-up is unsustainable. There is little evidence for the follow-up of gynaecological cancers and alternative strategies are urgently required.

Objective: To ascertain the needs of patients attending gynaecological cancer follow-up clinics in South-East Wales (SEW) and to explore the potential for alternative strategies of follow-up acceptable to patients.

Design: The outcome of every gynaecological cancer follow-up appointment during February 2011 in SEW was audited. Questionnaires were given to patients attending these clinics to ascertain their views on the acceptability of alternative methods of follow-up.

Results: 254 appointments were audited and 42 questionnaires collected. 76% of follow-up consultations were consultant-led with the outcome of 39% being 'patient well, no action taken'. The largest proportion of patients attending for follow-up were endometrial cancer patients: 48% of these were well. 56% of respondents would accept no formal follow-up but rapid access back to a specialist if symptomatic, 46% of patients would accept follow-up with a specialist nurse.

Conclusions: A large proportion of patients attending gynae-oncology follow-up clinics are well and no intervention is required. There is scope for alternative methods of follow-up in addition to consultant led clinics which could increase the efficiency of services. A rapid access clinic and telephone consultations could be explored in ovarian cancer follow-up and a nurse-led clinic could be useful in endometrial follow-up. Alternative methods of follow up for survivors of gynaecological cancers are required and with adequate explanations new strategies are acceptable to patients.
Poster Session III

INTENSIVE CARE UNIT ADMISSION AFTER GYNECOLOGIC ONCOLOGY SURGERY IN A BORDER HEALTH CARE SETTING

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Objectives: The objectives of this study were to identify pre- and peri-operative factors that could help predict admission into the Intensive Care Unit (ICU) after gynecologic oncology surgery in an academic border tertiary care hospital.

Methods: A retrospective cohort study was conducted to identify predictors of admission into the ICU after gynecologic surgery for reproductive tract malignancies from January 2007 - September 2011. Patient demographics, comorbidities, cancer diagnosis, operative data, and ICU outcomes were extracted from medical records. Adjusted odds ratios (OR) were calculated from a logistic regression model. Firth’s bias correction was used in the analyses of predictors.

Results: Of 99 patients that had major gynecologic surgery, 33 (33.3%) met the criteria of admission to the ICU. Median age was 55 y (range: 25-95 y). The majority of the cohort was Hispanic ethnicity 63.6%. Patients were more often obese 55.7%. Twelve predictor variables were included in the logistic regression analyses. Hispanic ethnicity (OR=21.24, P=0.051), the presence of ascites (OR=27.05, P=0.02), and bowel resection (OR 21.33, P=0.059), were associated with an increased risk of ICU admission.

Conclusions: There was a significant risk associated with Hispanic ethnicity and presence of ascites on admission to the ICU after gynecologic cancer surgery. This disparity may help create a high-risk profile that could serve to identify patients who require special counseling or services prior to major surgery.
Poster Session III

A COMPREHENSIVE ASSESSMENT OF SUPPORTIVE CARE AND SEXUAL HEALTH NEEDS AND READINESS FOR HELP IN SURVIVORS OF GYNAECOLOGICAL CANCERS

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Background: The percentage of patients surviving cancer has significantly increased. The need to better address patient needs beyond treatment has been recognized. However, research describing survivorship needs and readiness for help among women treated for gynaecological cancer (GC) is limited.

Objectives: To explore

1) supportive care and sexual health needs of women treated for a GC,

2) respondents’ readiness for help, and

3) types of services women desire to meet their needs.

Methods: Descriptive, cross sectional design based on principles of needs assessments. The Supportive Care Needs Survey (SCNS; Steele and Fitch, 2008) and the Sexual Health-Vaginal Changes questionnaire (SVQ; Jensen et al., 2004) were utilized.

Results: A total of 106 questionnaires were returned at the time of abstract submission. Half of the respondents were diagnosed with ovarian cancer, followed by endometrial cancer. Preliminary findings reveal that participants’ moderate to high post-treatment needs were: Fear of cancer recurrence, fear of cancer spreading, fatigue, sexual health needs, concerns about loved ones, uncertainty about the future, feelings about death and dying, and anxiety and fear about physical disability. Women reported wanting help with the most highly rated needs. They also want to be informed on what they can do to help themselves, and they want to have access to professional counselling.

Conclusion: These preliminary findings begin to describe the needs of women with GC after treatment, and suggest specific resources and interventions that may be helpful. The study is ongoing as we continue to recruit women with cervical, vulvar and vaginal cancers.
Poster Session III

IMPACT OF PELVIC RADIO-THERAPY ON GUT MICROBIOTA OF GYNECOLOGIC CANCER PATIENTS REVEALED BY MASSIVE SEQUENCING TECHNIQUE

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Introduction: There is no current clinical or experimental information on the impact of radiation to gut microbiota in cancer patients, we conducted a pilot observational study on the gut microbiota in patients receiving pelvic radiotherapy.

Methods: The study involved 9 gynecologic cancer patients who underwent 5 weeks of radiotherapy. Four fecal samples (before, during, at the end, and follow-up) were collected from each individual. The overall composition and alteration of gut microbiota in cancer patient receiving radiation were investigated by 454 pyrosequencing with barcoded primers targeting the V1/V2 region of the bacterial 16S rRNA gene.

Results: A total of 104,242 high quality reads covering each sample with average 2,217 reads was analyzed. UPGMA and PCoA of the gut microbial composition showed significant differences (P<0.001) between cancer patients and healthy individuals when compared with previously published massive sequencing data of health women. The number of observed and estimated species level taxon (97% sequence similarity cut-off) was severely reduced (P<0.003) and the relative abundance of each member largely changed and converged into narrow point after the radiation therapy. Especially phylum Firmicutes and Fusobacterium were severely affected by irradiation: 7% depression in Firmicutes and 4% increment in Fusobacterium.

Discussion: In this set of patients, we found dysbiosis of gut microbiota could be linked to health status and showed the impact of irradiation to gut microbiota in cancer patients. This study may be of help to treat cancer patient suffered by complication after radiation therapy.
Poster Session III

EFFECT OF LUMBAR SYMPATHETIC GANGLION BLOCK IN PATIENTS WITH LYMPHEDEMA AFTER THE TREATMENT OF GYNECOLOGIC CANCER: A PRELIMINARY REPORT

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Objective: To evaluate the effect of lumbar sympathetic ganglion block (LSGB) in patients with lymphedema after the treatment of gynecologic cancer.

Method: We performed LSGB to seven patients who had suffered from severe lower-extremity lymphedema after radical surgery and/or irradiation. The circumference of each thigh was measured at the uppermost portion of thigh in standing position. The level of discomfort from symptoms was estimated by visual analog scale (VAS) from 0 (absent) to 10 (very severe). We compare the initial circumference of thigh and VAS score with those of one day after intervention.

Results: After the block, lymphedema was relieved dramatically in some patients; Overall response rate was 71.4% (5/7), and average reduction of thigh circumference was 1.3cm (1-2) at the next day. Initial VAS score (mostly 3-5) was dropped to 0 or 1 after intervention. As expected, patients who experienced the response were strongly hoped to receive LSGB again in the future. Lastly, there were no complications associated with LSGB.

Conclusion: LSGB may be very effective in some patients with lymphedema after gynecologic cancer treatment. Clinical studies should be performed to validate the effect and safety of LSGB as a therapy for intractable lower-extremity lymphedema.
Poster Session III

THE ROLE OF SOLIFENACIN SUCCINATE IN THE MANAGEMENT OF BLADDER DYSFUNCTION IN RADICAL HYSTERECTOMY PATIENTS

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Introduction: Urinary bladder dysfunction, a common problem encountered after radical hysterectomy for gynecologic malignancies, is conventionally managed with prolonged bladder catheterization. This, however, is associated with patient discomfort, higher incidence of urinary tract infection, delayed ambulation and moderate cost.

Objective: This nonblinded, no placebo, randomized controlled trial was conducted to determine the efficacy and safety of solifenacin succinate in decreasing the mean duration of indwelling catheterization after radical hysterectomy.

Methodology: Patients 19 years old and above, diagnosed with early stage cervical cancer and stage II endometrial cancer were randomized to 2 arms: control arm and treatment arm (given 5 mg solifenacin succinate daily after radical hysterectomy). Bladder function testing was done on the third postoperative day and weekly thereafter. Indwelling catheter was removed once recovery of bladder function was diagnosed. Primary endpoint was the mean duration of indwelling catheterization until bladder function recovery was obtained. Patients were monitored for presence of urinary tract infection and adverse drug reactions.

Results: Each arm had 18 patients, with no statistically significant differences in the clinico-surgico-pathologic profile of patients. The mean duration of indwelling catheterization was significantly shorter in the treatment arm (13.33 days ± 10.50 SD) than in the control arm (21.33 days ± 11.66 SD) (p = 0.046). No adverse drug reactions were noted.

Conclusion: Solifenacin succinate effectively and safely reduced mean duration of indwelling catheterization among patients who underwent radical hysterectomy.
Poster Session III

EVALUATION OF THE RELATION BETWEEN PATIENT CHARACTERISTICS AND THE STATE OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING


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Purpose: Chemotherapy-induced nausea and vomiting (CINV) are major adverse effects of cancer chemotherapy. Paclitaxel and carboplatin are moderately emetogenic chemotherapeutics widely used for gynecologic cancer. The aim of the present study was to retrospectively evaluate the correlation between state of CINV and the characteristics of patients who received paclitaxel and carboplatin.

Patients and methods: We evaluated patients diagnosed with gynecologic cancer and received granisetron 3 mg and dexamethasone 20 mg on day 1 as antiemetic therapy with paclitaxel 175 mg/m^2 and carboplatin AUC=5 between April 2007 and March 2010. Data were collected from a patient questionnaire including items such as age, motion sickness, and hyperemesis gravidarum.

The logistic regression model was used to calculate the significant factors influencing CINV.

Results: 89 patients were enrolled. Motion sickness (odds ratio [OR] 3.61; 95% confidence interval [CI] 1.14 to 11.37), hypertension (-) (OR 20.37; CI 2.81 to 147.51) and chemotherapy in the adjuvant setting (OR 4.93; CI 1.48 to 16.41) were significantly correlated with grade 1 or more vomiting. In 78 patients who had given birth, hyperemesis gravidarum (OR 4.17; CI 1.11 to 15.65) and hypertension (-) (OR 10.37; CI 1.71 to 62.87) were significantly correlated with grade 1 or more vomiting.

Conclusions: The findings of the present study suggest that the frequency of grade 1 or more vomiting are increased in patients with motion sickness, hypertension (-), adjuvant chemotherapy, and hyperemesis gravidarum that are receiving paclitaxel and carboplatin. Those patients should receive aprepitant or palonosetron instead of granisetron as antiemetic therapy.
Poster Session III

EFFICACY OF LAFUTIDINE, A HISTAMINE H2-RECEPTOR ANTAGONIST, FOR TAXANE-INDUCED PERIPHERAL NEUROPATHY IN THE PATIENTS WITH GYNECOLOGIC MALIGNANCIES

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Objectives: Lafutidine, one of the antagonists of histamine H2-receptor, has gastroprotective activity associated with activation of capsaicin-sensory nerves. We investigated the efficacy of lafutidine for peripheral neuropathy caused by taxanes in the patients with gynecological malignancies.

Patients and methods: Twenty patients with taxane-induced peripheral neuropathy in the treatment of gynecological malignancy entered this study. After informed consent had been obtained, lafutidine (20 mg per day) was administered orally. Efficacy of lafutidine was accessed according to the Patient Neurotoxicity Questionnaire (PNQ) item 1.

Results: The observed efficacy of lafutidine was as follows: significant effect in four patients, moderate effect in five patients, slight effect in five patients, and no effect in six patients. The efficacy including significant to slight effect was observed in 70% of patients (95% confidence interval, 48.1% to 85.5%). Any obvious adverse effects due to lafutidine have never been observed.

Conclusions: This pilot study demonstrates relatively high efficacy of lafutidine for taxane-induced peripheral neuropathy. Further prospective studies are warranted.
Poster Session III

HORMONE REPLACEMENT THERAPY IN REHABILITATION OF PATIENTS WITH GYNAECOLOGICAL CANCER

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During last years number of patients with gynecological malignancies in reproductive and premenopausal age has been permanently increasing. In majority of cases radical treatment results in termination of ovarian function and development of post ovariectomy syndrome.

The aim of the study was to follow the degree of post ovariectomy syndrome after radical treatment and evaluate efficacy of hormone replacement therapy in patients with gynecological malignancies.

Results of hormone replacement treatment were analyzed in following groups of patients: 30 patients with endometrial cancer, 43 patients with cervical cancer after surgical treatment (or surgical treatment + irradiation); 15 patients with ovarian cancer after complex treatment.

The age of patients amounted from 23 to 52 years. The duration after operation lasted 6.7 ± 1.2 month. Transdermal hormone replacement therapy was prescribed to patients during 3-4 month after operation following by ordering the tablets. The duration of the treatment amounted from 3 month to 5 years. The evaluation of hormone replacement therapy effectiveness was made according to modified menopausal index. All patients before surgical treatment had menstruation.

Results: Vegetative-vascular disorders of different levels have been observed in every patient at the beginning of observation. Hormone replacement therapy was found to be effective in correction of the menopausal symptoms. Urogenital disorders (dryness in vagina, dysuric phenomenon) appeared to be decreased by 65-70 %. Pronounce psycho-emotional disorders in patients were decreases by 60-63% as compared with control group.

Conclusion: Prescription of hormone replacement therapy in patients with gynecological malignancies supports increased quality of life.
Poster Session III

DETERMINATION OF THE D-DIMER CUTOFF LEVELS FOR MAKING A DIAGNOSIS OF VENOUS THROMBOEMBOLISM BEFORE AND AFTER GYNECOLOGIC SURGERY

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Objective: The current study was intended to determine the appropriate cut-off values for plasma D-dimer (DD) levels for making a diagnosis of venous thromboembolism (VTE) before and after gynecologic surgery.

Methods: A total of 1232 patients underwent gynecologic surgery between January 2006 and December 2008. Receiver operating characteristic (ROC) curves analysis was used to determine the appropriate preoperative DD cut-off levels. Patients at a high risk for VTE received anticoagulant therapy with danaparoid sodium 1250 U/day for 5 to 7 days between January 2006 and June 2008 and with fondaparinux sodium 2.5 mg/day for 7 days from July 2008 onward. DD levels were measured on postoperative days 1, 4, 7 and 10.

Results: When 3.0 µg/ml was set as the preoperative DD cutoff level. These values were considered to be optimal and the preoperative DD cutoff level was determined to be 3.0 µg/ml. In patients not administered anticoagulant therapy, when 7.1 µg/ml on postoperative day 4 was set as the postoperative DD cut-off level. These scores were considered to be optimal and the postoperative DD cut-off level was determined to be 7.1 µg/ml. In patients treated with danaparoid sodium, when 12.3 µg/ml on postoperative day 4 was set as the postoperative DD cut-off level. These values were considered to be optimal and the postoperative DD cut-off level was determined to be 12.3 µg/ml for patients under treatment with danaparoid sodium. Conclusion: Determination of the preoperative and postoperative DD cut-off levels may contribute to making an early diagnosis of VTE.
Poster Session III

OUTCOMES FOLLOWING PLACEMENT OF PERCUTANEOUS GASTROSTOMY TUBE (PGT) FOR BOWEL OBSTRUCTION IN OVARIAN CANCER

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Malignant bowel obstruction (MBO) affects 25-50% of women with recurrent ovarian cancer, ultimately resulting in death. As goals of therapy shift to palliation, placement of a PGT is a feasible and safe option. The objective of this study was to evaluate survival outcomes of patients undergoing PGT placement with recurrent ovarian cancer.

Retrospective chart review was used to identify patients with epithelial ovarian cancer who underwent PGT placement from 2002-2010. Kaplan-Meier methods were used to estimate the median survival and cox proportional hazard regression used to determine if any variables were associated with the hazard of death.

Fifty-three patients met inclusion criteria. Median length of diagnosis prior to PGT was 21 months. Seventeen (32%) patients experienced one or more complications; revision (9), leakage/fistula (5), blockage (5), infection (8). Fifty (94%) experienced relief of symptoms after placement. Fourteen patients tolerated a soft/regular diet, 34 liquid, 2 tube feeds, and 2 none. Following placement, 36% patients received additional chemotherapy and 40% received total parental nutrition (TPN). Thirty-five patients were discharged home/outpatient facility, 16 to hospice care, and 2 died post-operatively. Median survival (MS) for all patients was 46 days. Patients who received chemotherapy had a MS of 169 days compared to 33 days (p< 0.001). Survival was not impacted by TPN, platinum sensitivity, performance status, or year of treatment.

A majority of patients with MBO can be successfully palliated with PGT. Given that the median survival is approximately 46 days, aggressive cancer therapy after PGT placement should be individualized.
Poster Session III

QUALITY OF LIFE AMONG CAREGIVERS OF PATIENTS WITH GYNECOLOGIC CANCER IN TURKEY

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**Purpose:** In this study, the aim was to examine the quality of life of caregivers of patients with gynecologic cancer.

**Method:** The cross sectional study has been conducting in a gynecology clinic at a state Oncology Education and Research Hospital, in Turkey. Caregivers of inpatients with gynecologic cancer have been included in the sample of study. Data has been collecting using a questionnaire that included socio-demographic questions for caregivers and the Turkish version of the Caregiver Quality of Life Index-Cancer (CQOLC).

The study is still in progress and to be completed by September 2012. (This cross sectional study will be conducted for a year). Statistical analysis was performed for data collected from 87 caregivers for the present.

**Results:** Patients diagnosed with endometrial, cervical, ovarian cancer. The majority of them diagnosed with ovarian cancer (63.2%). The average age of the caregivers was 41.03±1.31, and 74.4% were female. Daughters made up 40.2% of family caregivers; spouses and siblings (14.9%) were the next most frequent relationship to the patient. Only 31% of caregivers shared the caregiving process with someoneelse. The mean score ± SD of the Total CQOLC was 57.87±19.02 (range 8.0±98.0), and scores of the four subscales were as follows: Burden 17.93±8.88 (1.0±40.0), disruptiveness 14.50±5.34 (3.0±24.0), positive adaptation 16.91±5.12 (3.0±24.0) and financial concerns 8.51±2.98 (1.0±12.0).

**Conclusion:** Depending upon all data collected at end of the study, statistical anlysis is performed andrecommendations are to be made, afterwards.
Poster Session III

GYNECOLOGICAL MALIGNANCIES IN THE OLDEST OLD: PATTERNS OF CARE AND OUTCOME

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Objective: In recent years, it is said that cancer treatments equivalent to younger patients can be conducted for elderly patients with good general status. In the present study, we examined our current treatment and outcome for patients at the age of 75 or older.

Methods: Twenty-nine cases (14 cervical cancer; 8 endometrial cancer; 7 ovarian cancer) at the age of 75 or older that underwent initial treatment from January 2008 to December 2010 were examined for the patterns of care and outcome.

Results: The mean age was 80.5 years old and the ECOG performance status (PS) score was 1 in 25 cases and 2 in 4 cases. Radiation therapy was conducted for all cases of cervical cancer. Surgical treatment was conducted for all cases of endometrial and ovarian cancer but 6 cases had cytoreductive surgery. Although chemotherapy was conducted with taxane and platinum for 7 cases after their surgical treatment, grade 3 or 4 neutropenia was recognized in 5 cases. Standard treatment was executed in 16 (55%) out of 29 cases.

Conclusion: For elderly cancer patients with good PS and no severe complication, it is considered that treatments equivalent to younger patients can be conducted. However, it is necessary to sufficiently assess efficacy and tolerability before treatments and provide more careful care during the treatments.
Poster Session III

PREOPERATIVE DIAGNOSIS OF PRIMARY FALLOPIAN TUBE CARCINOMA

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Objective: Primary fallopian tube carcinoma (PFTC) is one of the least common gynecological cancers and is difficult to diagnose preoperatively. Therefore, the present study investigated the modalities for detection of PFTC, including clinical symptoms, Pap smears, imaging findings and tumor markers.

Subjects: We reviewed 23 PFTC patients who underwent surgery at our institution between 1991 and 2010.

Results: The median age was 60 years (range, 46 – 75 years). 6 of the 23 patients were nulliparous and 17 were pluriparous. 22 patients were postmenopausal. The presenting signs of PFTC was lower abdominal pain (n = 7, 30%), vaginal bleeding (n = 5, 22%), and abdominal bloating (n = 4, 17%). Positive cervical, endometrial cytology and endometrial biopsy were found in 8 (34.8%), 11 (50%) and 6 (54.5%) cases, respectively. The positive rate of endometrial cytology was 40% with each clinical stage. Positive rate of CA125 was 82.6% and serum CA125 levels were found to be elevated with clinical stage. Among 23 cases, just 3 cases could be suspected or diagnosed correctly preoperatively. Two of them were based on MRI, and one of them was on positive endometrial cytology which was considered to be extrauterine adenocarcinoma. Among 23 PFTC cases, 15 cases were misdiagnosed as ovarian carcinoma.

Conclusion: Abnormal MRI findings are often absent in PFTC, making preoperative diagnosis difficult. The present findings indicate that we should suspect PFTC in cases with positive endometrial cytology and elevated CA-125 levels with no lesion in endometrium, and should review the imaging studies of MRI carefully.
Poster Session III

A STUDY OF PERCUTANEOUS CT-GUIDED DRAINAGE FOR POSTOPERATIVE SYMPTOMATIC LYMPHOCYSTS AFTER RETROPERITONEAL LYMPHOADENECTOMY


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Objective: To assess whether percutaneous CT-guided drainage for postoperative symptomatic lymphocytes was beneficial.

Patients and method: Between April 2011 and February 2012, six patients (2 cervical cancer, 1 endometrial cancer, 3 ovarian cancer) who had symptomatic lymph cysts were underwent drainage. Retrospective medical chart review were performed.

Result: Operation procedures were 2 radical, 1 semiradical, and 2 simple hysterectomy. Extents of lymphadenectomy were 2 of pelvic lymphadenectomy and 4 pelvic and paraaortic regions. Lymphocysts occurred at left pelvic lesion in all 6 cases. The median of major axis was 88mm (range 55-98mm). The indications of drainage were 3 abscess formation, 2 abdominal pain, and 1 lower abdominal distention. 5 cases ware punctured from the back and 1 cases from the abdomen. The median time from lymphadenectomy to drainage was 93 days (range 15-1118 days). The median time of keeping drain was 8days (range 5-15 days). All cases took complete relief of symptoms. In 3 cases of lymph abscess, the median peak body temperature, white blood cell count, and CRP before drainage was 39.3°C, 12900/µl, and 25.9 mg/dl, respectively. We used antibiotics and drainage in all 3 cases. The median time of fever going down under 37°C from drainage was 3 days, the median time of WBC going down under 8000/µl was 3 days, and the median time of CRP going down under 1.0mg/dl was 14 days. There were no recurrence of abscess in all 3 cases.

Conclusion: Percutaneous CT-guided drainage for postoperative symptomatic lymphocysts was effective.
Poster Session III

DERMATOMYOSITIS (DM) AND FALLOPIAN TUBE CANCER (FTC)

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Dermatomyositis (DM) is an idiopathic inflammatory myopathy associated with characteristic cutaneous and extracutaneous manifestations, and an increased incidence of internal malignancies, notably cancers of the female genital tract esp. in patients > 60 years.

Mrs MP, 60 years, presented with acute Dermatomyositis (florid skin rash, proximal muscle weakness & dysphagia) & postmenopausal bleed (PMB). Some improvement noted in muscle strength with steroids.

Investigations s/o complex pelvic mass, CA125: 42u/ml

EUA, Hysteroscopy, EB & guided biopsy of pelvic mass high up in post fornix. HPE: Mod to poorly differentiated adenocarcinoma +ve for CK7, focal +ve for S100, neg for CK20. Inactive endometrial curettings.


Punch biopsy forearm: s/o Dermatomyositis.

Uncomplicated recovery. Carboplatin postop. By 2nd cycle, rash nearly gone & walking around the house. Rash recurred with 3rd cycle. Settled with Prednisolone 7.5 mg OD

Follow up CT Scans- No e/o recurrence.

Dermatomyositis settled. CA 125 - 15, CTscan - normal.

An association between DM and FTC may exist because of significant improvements in DM after tumor removal and chemotherapy. Knowledge of this association may help in early diagnosis, improved management & better outcomes for patients.
Primary Epithelioid Hemangioendotheioma of the Retroperitoneum: Report of a Rare Case

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Introduction: Epithelioid hemangioendothelioma (EHE) is a rare type of malignant tumor of vascular endothelial origin, and can arise from various tissues, including soft tissue, bone, liver, and lung. It is considered to be intermediate between hemangioma and angiosarcoma. However, according to its relatively high rate of metastasis, EHE, is now classified in the malignant category.

Case presentation: We present a case of a 40-year-old female patient who presented to our clinic diagnosed with an enormous pelvic tumor complaining about pain and pressure in the peritoneal cavity. The imaging findings revealed an enormous solid tumor occupied almost the whole peritoneal cavity. The tumor was penetrated both the ureters and the huge region vessels. As a result, the tumor was described as unresectable. The histological examination of the omentum and sections of the tumor revealed a mesenchymal neoplasm originated from the vessels, compatible with epithelioid hemangioendothelioma. Afterwards the patient received sessions of systematic chemotherapy and radiation therapy.

Discussion: EHE is a rare malignant tumor of intermediate grade and unpredictable behavior. When it is originated from the retroperitoneum, is extremely rare, and only a few cases have been reported. EHE in our case was suspected to have been derived from small vessels in the retroperitoneal space. The neoplasm usually presents as solitary, rarely, slightly painful erythematous papules, nodules, plaque and nonhealing ulcer. Chemotherapy and radiation therapy have been proposed especially for unresectable tumors. For successful surgical resection, early detection of the tumor is necessary and obligatory.
Poster Session III

ONDANSETRON, METOCLOPRAMIDE AND DEXAMETHASONE FOR POSTOPERATIVE NAUSEA AND VOMITING (PONV) PROPHYLAXIS FOLLOWING MTP AND LAPROSCOPIC TUBAL LIGATION

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Background: Overall incidence of PONV (25 - 43%) following general anaesthesia remains unacceptably high. It is still higher (50 - 80%) for Gynecological Laparoscopic Surgeries and warrants an urgent need to find an ideal antiemetic for prophylaxis from PONV.

Aims: Evaluate ondansetron, metoclopramide and dexamethasone for PONV prophylaxis.

Methods: In a randomized, prospective, double blind study we compared the antiemetic efficacy of Ondansetron (4mg), Metoclopramide (10mg) and Dexamethasone (8mg) when given alone and when Dexamethasone was given in combination with either Ondansetron or Metoclopramide in 120 female patients undergoing diagnostic gynecological laparoscopy under general anaesthesia. Incidence of nausea and vomiting (N/V) was assessed at half hourly intervals for 4 hrs postoperatively using visual analogue scale (VAS). It was graded as mild (VAS< 5) moderate (VAS=5) and severe (VAS >5).

Results: The study revealed that Ondansetron (group I); Metoclopramide (group II) and Dexamethasone (group III) were significantly better than placebo (group VI) in controlling PONV (p < 0.05) but no difference was found when compared to each other. The efficacy of combination groups i.e. Ondansetron plus Dexamethasone (group IV) and Metoclopramide plus Dexamethasone (group V) was comparable to each and significantly better than placebo (p < 0.01). Though by itself Dexamethasone is ineffective, but it significantly enhanced efficacy of other drugs when given in combination (p < 0.05).

Conclusion: The combination of Dexamethasone with Ondansetron or Metoclopramide is more reliable and superior antiemetic than either of these drugs administered alone.
Poster Session III

IS GENOTYPING OF UGT1A1 REALLY USEFUL FOR GYNECOLOGIC CANCER PATIENTS TREATED WITH IRINOTECAN-BASED CHEMOTHERAPY?

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Background: Genotyping of UGT1A1*28 and *6 was supported by national insurances since 2008 in Japan, however, there still exists argument which patients receive the test.

Material and methods: Medical records of gynecologic patients treated with irinotecan-based therapy between 2003 and 2010 in our hospital were reviewed. Before 2007, dose reduction of irinotecan was based on physical status or previous myelosuppression (Non-UGT group). Since 2007, doses of irinotecan were modified by choice of physicians according to UGT1A1*28/*6 genotype (UGT-group). Adverse effects at the 1st cycle were compared.

Results: 178 cases were treated with irinotecan-based therapy: 52 with cervix, 16 with uterine corpus, and 110 with mullerian cancers. 70 patients underwent UGT1A1 genotyping: 41 (59%) with wild-type, 27 (39%) with hetero-type, and 2 (3%) with homo-type/double hetero-type. Irinotecan dose was modified in 24% in UGT group, and 11% in non-UGT group. In UGT group, Grade3/4 non-hematologic (14% vs. 26%, p=0.06) and Grade4 hematologic toxicities (7% vs. 19%, p=0.01) were reduced. Grade4 non-hematologic toxicities were not observed in UGT-group (0% vs. 6%, p=0.04).

Conclusion: Tailor-made chemotherapy according to UGT1A1 genotyping enabled us to reduce severe toxicities in gynecologic patients treated with irinotecan. Further investigations including response rates at reduced doses are needed to facilitate UGT1A1 genotyping.
Poster Session III

EFFECTIVENESS AND THE SAFETY OF THE XA INHIBITOR (FONDAPARINUX) IN THE VTE TREATMENT IN THE GYNECOLOGICAL DISEASE


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Objective: The current standard initial therapies for VTE are low-molecular-weight heparin (LMWH) and unfractionated heparin (UH). In a dose-ranging study of patients with symptomatic VTE, Xa inhibitor (fondaparinux) had efficacy and a safety profile similar to those of LMWH. We investigated the effectiveness and the safety of the Xa inhibitor (fondaparinux) in the VTE treatment in the gynecological disease.

Methods: The subject cases were 11 patients with VTE who underwent the treatment with fondaparinux.(two cervical cancer, four endometrial cancer, four ovarian cancer, and one vulval cancer) As to the details of VTE, the numbers of DVT only, PTE only, and DVT+PTE were 2, 4, and 5 respectively. For the diagnosis of VTE, serum D-dimer level, helical CT, and ultrasound diagnosis of lower limbs were used. In addition to the 7.5mg of fondaparinux (subcutaneous administration) which was started at the onset of VTE, warfarin was simultaneously administered from the 3rd day of onset, and the fondaparinux was discontinued when the warfarin reached the effective therapeutic range.

Results: The mean value of D-dimer at the onset of VTE was 13.6±9.1, while that of the 3rd day of the treatment was 6.6±5.0, thus it was significantly decreased by the administration of fondaparinux. (p< 0.01) It took 5.1±4.6 days in average for the warfarin to reach the effective therapeutic range. And in none of the cases, adverse event such as major bleeding was observed.

Conclusion: Although the number of cases was still as few as 11, Xa inhibitor (fondaparinux) for the treatment in the area of gynecology was effective and safe.
SURVIVORSHIP IN OVARIAN CANCER: A PILOT STUDY TO ASSESS THE DIVERSE NEEDS OF OVARIAN CANCER SURVIVORS

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Introduction: Ovarian cancer is a diverse disease. Little data exist on quality of life (QOL) for survivors. Our goal was to determine priorities for future resources and the best means to provide support for survivors.

Methods: The EORTC QLQ-C30 and OV28 QOL and one investigator-derived survey measuring access to and experience with computer/online resources were administered in an outpatient pilot initiative. Clinical parameters were abstracted and tested for associations with questionnaire responses.

Results: 103 women consented/completed all components. Mean age was 58 (range 29-85yrs), with 95% having epithelial ovarian carcinoma, 66% high grade serous, and stage I (28%), II (15%), III (47%), and IV (10%) represented over the primary treatment (24.5%), surveillance (46%), recurrent (22.5%), and palliative (7%) phases of the survivorship continuum. 82% of respondents preferred to participate with paper/written surveys vs. in-person (8%) or electronic/tablet (10%), however 95% have computer access at home, with 70% describing daily use. 51% characterize their disease burden as “quite a bit” or “very much” which did not vary by histology/diagnoses. 70% have sleep disturbances. Peripheral neuropathy and other chemotherapy side effects were negatively associated with age (p=0.024 both). Cardiovascular (CV) and respiratory comorbidities influenced EORTC scores in physical functioning (p=0.027/0.041), global QOL (p=0.03/0.039), and sexual health (p=0.025 CV only). Task completion/memory/concentration, anxiety and fatigue were the top distress categories prioritized by respondents yet were rarely discussed (< 11%) in clinical follow-up.

Conclusions: A diverse range of age, diagnoses, prognoses, comorbidities, and resources impact the ovarian cancer survivorship journey and need to be considered in designing appropriate support and interventions for this disease.
Poster Session III

PRECISE EVALUATION OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY USING VISUAL ANALOGUE SCALE: A QUANTITATIVE AND COMPARATIVE ANALYSIS WITH PACLITAXEL-CARBOPLATIN AND DOCETAXEL-CARBOPLATIN THERAPY

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Objective: The aim of this study was to investigate chemotherapy-induced peripheral neuropathy (CIPN) using the visual analogue scale (VAS) and compare CIPN in paclitaxel and docetaxel chemotherapy.

Methods: We asked 93 patients with gynecologic cancer who received paclitaxel (175 - 180 mg/m²) and carboplatin (AUC 5 - 6) (TC) or docetaxel (60 - 70 mg/m²) and carboplatin (AUC 5 - 6) (DC) to fill out a questionnaire about pain in muscles or joints and numbness in limbs using VAS. Totally 134 cycles of TC and 79 cycles of DC were evaluated. We analyzed the daily change of VAS scores (0-10) every 10 days, and compared scores according to the regimen. VAS scores were compared in every 2 cycles to examine cumulative toxicity.

Results: Daily changes of CIPN for each therapy could be demonstrated in detail. Pain and numbness had separate patterns of appearance as follows. VAS scores of pain rose rapidly during the first 4 days and declined to similar level as day 1 in 10 days. VAS scores of numbness rose gradually in the first 6 days. A greater VAS scores were seen in TC patients than in those of DC patients throughout 10 days. As the number of cycles grew, accumulating neuropathy was clearly found in TC patients.

Conclusions: This result suggests that CIPN can be estimated precisely using VAS system. The difference of CIPN between TC and DC was clearly observed by the quantitative analysis.
Poster Session III

MONITORING CHEMOTHERAPY CARDIOTOXICITY: HOW EVALUATE IT?

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Cardiovascular complications in oncologic patients are becoming a relevant problem because of combined therapy and improvement in overall survival. We developed a score to assess treatment related risk and monitor cardiac function.

Between March 2011 and March 2012, 108 patients were enrolled at the Department of Gynecologic Oncology, Mauriziano Hospital, Turin. Clinical data, blood and cardiologic tests were used to classify patients and evaluate them during treatment.

Patients were affected by gynecological cancer (35%) and breast cancer (65%). They were treated with regimen containing anthracyclines (50%), taxanes (58%) and both drugs (26%). A monoclonal antibody was administered in 17% of cases. Individual cardiovascular risk was calculated considering age (mean 56 years), weight (mean 63.7 kg), height (mean 162 cm), total and HDL cholesterol (mean 213 and 53 respectively), diabetes (6%), hypertension (28%). Cardiovascular risk related to specific treatment was low in 52% of women. Global risk was low in 52%, mild in 47% and high in 1% of patients. Low risk patient were submitted to ECG and echocardiography every three months: no alterations were recorded. Mild and high risk were submitted to low risk protocol and BNP and troponine dosage at day 0 and 1 of chemotherapy infusion. BNP increased in six patients (5%) and it was associated to increased troponine in other 4 women (4%): none discontinued the treatment. One women was submitted to coronarography before starting treatment.

Early cardiovascular complications in oncologic patients are uncommon. Further studies are needed to evaluate how monitoring patients after treatment.
Poster Session III

CLINICAL USEFULNESS OF CART FOR TERMINALLY ILL CANCER PATIENTS WITH REFRACTORY MASSIVE ASCITES

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Cell-free and concentrated ascites reinfusion therapy (CART) is intended to treat patients by ultrafiltration and reinfusion of their refractory ascites. In CART system, bacteria and cancer cells in removed massive ascites are filtrated. Then, water is removed in the condenser, resulting in higher protein concentration. The purpose of this study was to assess the clinical usefulness of CART in the treatment of refractory massive ascites in patients with peritonitis carcinomatosa.

CART was performed 6 times for 4 patients with terminally ill cancer. Autologous protein with higher concentration was intravenously administered. The amount of aspirated ascites and albumin concentration were 3,153±1,083 mL (1,265-4,500 mL) and 1.9±0.7 g/dL, respectively. Recovered fluid volume by CART, condensed albumin, and albumin concentration rate were 519±272 mL (100-860 mL), 9.9±1.3 g/dL, and 80.5±6.7%, respectively. CART was effective in maintaining serum albumin concentration, and it is possible to repeat infusion. During CART, patients’ performance status was 1-2 and vital signs were stable except for mild elevation of body temperature. Daily life was maintained without serious side effects.

Use of CART for terminally ill cancer patients with refractory massive ascites due to peritonitis carcinomatosa contributes to the improvement of patients’ quality of life and symptoms relief. With autologous infusion of condensed ascites, patients can avoid infection, allergy reaction, and receive of expensive blood products.
Poster Session III

PERMANENT PERITONEAL CATHETER INTRODUCED UNDER ULTRASOUND GUIDANCE AS A PALLIATIVE DERIVATION OF TORPID ASCITES

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Objectives: We present our experience with permanent peritoneal catheter as a palliative support in patients with only symptomatic treatment and resistant ascites requiring frequent paracentheses.

Methods: We prospectively evaluated operartional and clinical parameters and outcome in patients who underwent permanent peritoneal catheter insertion under ultrasound guidance for palliative derivation of ascites. We used pediatric catheter for peritoneal dialysis with two dacron cuffs tunnelized in subcutaneous tissue.

Results: The catheter was inserted in 12 patients under ultrasound guidance using combined local anesthesia and intravenous analgosedation, no general anesthesia was needed. The median of operational time was 21 minutes, procedure required half-day hospitalization. Patients started to emit the ascites (200-500ml) second postoperational day and continued every 2-3 days. Peroral protein supplementation was given. Ionts, renal and hepatic functions, albumin and total protein were monitored every 2 weeks. The average duration of catheter usage was 4 months. There were no infectious complications and no patient needed hospitalization due to hypoproteinemia or hypohydration.

Conclusion: We can recommend this procedure as well-tolerated and comprehensive support for incurable patients with torpid persistant ascites.

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THE EFFECT OF CONCURRENT CHEMO-PHOTODYNAMIC THERAPY (CCPDT) IN THE CASE OF FAILURE OF HORMON THERAPY IN ENDOMETRIAL CANCER FOR SPARING FERTILITY

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Introduction: Progestin has been used for sparing fertility in endometrial cancer. But when the hormone treatment fails, the classical methods as like surgery, chemotherapy and radiation should be performed. However these methods are not suitable in young women who want to preserve their fertility. Thus, we performed the photodynamic therapy with chemotherapy, which can remove the lesions and preserving fertility at the same time.

Methods: Two endometrial cancer patients (stage 1A, G1 and G2) who failed the treatment with Medroxyprogesterone Acetate (MPA) were selected. We used photodynamic therapy with carboplatin for treatment (Concurrent Chemo-Photodynamic Therapy, CCPDT). A photosensitizer (2.0mg/Kg, Photogem™[HpD], FINE chemical, Russia) was injected 48 hours prior to PDT followed by administration of carboplatin (75mg/m² IV) 3 hours before PDT. Then, we applied a non-thermal laser light (CERALASTM Diode Laser 632 System, biolitec, Germany) 250J/Cm² in the endometrium.

Results: All tests for endometrial cancer which were performed every 3 months showed complete regression in two patients. More than 50 months has been passed and so far, there was no evidence of recurrence. One of those delivered a child and the other try to get pregnant now.

Conclusion: Unlike the traditional cancer therapy, the CCPDT could cure the selective lesions without any destruction of reproductive organ simultaneously maintaining the fertility. Therefore, we can suggest that CCPDT could be an optional solution in the case of unresponsive result with hormonal therapy in the endometrial cancer patients who wants to get pregnant. However, we think that further clinical studies should be required.
Poster Session III

PROGNOSTIC FACTORS IN UTERINE SARCOMA: A CLINICOPATHOLOGIC AND IMMUNOHISTOCHEMICAL STUDY OF 30 CASES

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Background: Uterine sarcomas are a heterogeneous group of tumors that is divided into high grade and low grade sarcoma. The objective of this study is to examine the prognostic relevance of clinical, pathological and immunohistochemical features of this group of tumor.

Methods: The study include uterine sarcoma treated from 1994 to 2006. Twenty-two cases are high grade sarcoma. Clinical and pathological data were obtained immunostained with antibodies for p53, bcl-2, estrogen receptor (ER), Her2 and c-kit. The clinicopathological and immunohistochemical features were statistically analysed.

Results: The mean follow-up is 32 months. Twelve (55%) patients with high grade died of the disease and none in the low grade. In the high grade group, stage (p=0.01), myometrial invasion in early stage tumor (p=0.04), and lymphovascular invasion (p=0.043) were significant predictors of patient outcome in univariate analysis. Similarly, tumor cell type, ER, p53 and bcl-2 expression showed statistical significant correlation with tumor-specific survival (p=0.0039, p=0.001, p=0.03, and p=0.04 respectively). ER and bcl-2 expression were associated with better outcome and the opposite for p53 expression. In a multivariate analysis only the tumor stage and cell type had independent statistical significance (p=0.04 and p=0.035 respectively). Overexpression of p53 and Her2 were observed in 40% and 60% of carcinosarcomas respectively. The ER and bcl was expressed in the low grade sarcoma group.

Conclusions: This study demonstrates that stage and tumor cell type are the most important prognostic indicators of patient outcome in uterine sarcoma. However, Immunohistochemical failed to maintain significant association with patient outcome in multivariate analysis.
Poster Session III

UTERINE SEROUS CARCINOMA INVOLVING AN ENDOMETRIAL POLYP: A MULTI-INSTITUTIONAL STUDY

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Aim: To evaluate if uterine serous carcinoma (USC) confined to a polyp differs significantly from USC confined to the endometrium with respect to pathologic characteristics and clinical outcomes.

Methods: A retrospective multi-institutional review of USC cases from 1989-2011 was completed. Those cases with USC confined to a polyp and/or the endometrium without myometrial invasion were extracted and pathologic characteristics and clinical outcomes were evaluated.

Findings: USC cases meeting described parameters included 17 cases with disease confined to a polyp, 18 cases confined to the endometrium and 19 cases involving both a polyp and the endometrium. Stage I disease was found in 65% (N=11), 77% (N=13) and 94% (N=13) of cases in each group respectively. Tumor size >2cm was more common when disease involved the polyp alone (6/11) or the polyp and the endometrium (13/19) compared to the endometrium alone (3/18) (p=0.011). Angiolymphatic invasion was more common when USC involved the endometrium (39%) or the endometrium and a polyp (21%) compared to disease confined to a polyp (6%). Two of 11 patients in the group with USC involving the endometrium alone had lymph node involvement compared to no cases in the other groups. Recurrence rates were 18% (polyp alone), 26% (polyp and endometrium) and no recurrences in USC confined to the endometrium.

Conclusion: USC confined to a polyp less frequently has adverse pathologic features of angiolymphatic invasion and lymph node metastasis. However, a significant risk for recurrent disease persists when USC is confined to a polyp.
Poster Session III

SENTINEL LYMPH NODE MAPPING FOR ENDOMETRIAL CANCER

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Objectives: To evaluate detection rate, sensitivity and negative predictive value (NPV) of sentinel lymph node (SLN) mapping in endometrial cancer.

Methods: This single center study identified all patients undergoing hysterectomy, salpingo-oophorectomy, lymphadenectomy and SLN mapping for endometrial cancer between November 2010 and February 2012. Data was prospectively collected. Colorimetric and/or radio-isotopic detection with Patent Blue (PB) and Technetium (Tc99) were used to detect SLNs, followed by complete pelvic lymphadenectomy with or without para-aortic node sampling. Tc99 was injected on the morning of surgery, and PB after induction of anesthesia, at 3 and 9 o'clock. Intra-operative frozen section was optional. SLNs were ultra-staged for final pathology. Detection rate, sensitivity and NPV were calculated.

Results: Among 64 operated patients, SLNs were removed by laparoscopy in 62.5% of cases and laparotomy in 37.5%. At least 1 SLN was identified in 98.4% of PB cases (n=63) and 100% of Tc99 (n=32). Overall, 12.5% of patients had unilateral and 87.5% bilateral SLN identification. Fourteen patients (21.9%) had pelvic node metastasis including 10 macro-metastases, 2 micro-metastases and 2 isolated tumor cells (ITC). Concurrent metastatic para-aortic nodes were identified in 4 of those patients. Sensitivity of SLN mapping was 100% after ultra-staging (n=64) and 66.7% on frozen section (n=41), while NPV was 100 % and 91.4%, respectively.

Conclusion: SLN mapping in endometrial cancer appears promising. Detection rate is high. Although the sensitivity of intra-operative frozen section is limited, ultra-staging provides excellent sensitivity and NPV. Currently, the clinical significance and the management of micro-metastasis and ITC remains uncertain.
Poster Session III

ESTABLISHMENT OF PRIMARY ENDOMETRIAL CARCINOMA CELL CULTURES AS A PRECLINICAL TOOF FOR DRUG SCREENING: METHODS AND CHARACTERIZATION

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**Background:** Treatment options for primary advanced and recurrent endometrial cancer (EC) are limited, making development of new treatment strategies essential.

**Aim:** Our objective was to establish primary EC cell cultures to provide a cellular model for both in vitro and in vivo studies, including screening of new drugs.

**Methods:** After informed consent, fresh endometrial tumor biopsies were collected. Primary cell cultures were established after collagenase digestion and fibroblast depletion. They were validated by (i) measurement of telomerase activity, (ii) dynamic monitoring of cell proliferation (xCELLigence), and (iii) immunocytochemical stainings. In vivo tumorigenicity was determined in a s.c. xenograft model. Mutation analysis (Sequenom) was performed to detect hotspot mutations in genetic pathways that are known to be affected in EC (e.g. PI3K/PTEN/AKT and EGFR/KRAS). The mutation profile of the primary tumor, cell culture and xenograft was compared.

**Results:** Success rate for grade 2 and 3 tumors was ~30%. Telomerase activity of all cell cultures was similar to this of the HEC-1A cell line. Doubling time ranged between 19-28h. All cultures were negative for CD90 and α-SMA, positive for cytokeratin, whereas vimentin expression varied among cultures. In vivo tumorigenicity analysis showed tumor take rates between 60-100%. Mutational profiling identified PTEN, PIK3CA, KRAS, NRAS, BRAF and p53 mutations, which remained identical in the primary tumor, the cell culture, and xenograft.

**Conclusion:** We here present the first evidence for the establishment of primary EC cell cultures, providing an alternative, primary tumor-based model for in vitro and in vivo (targeted) therapeutic drug screening in EC.
Poster Session III

POSTOPERATIVE RADIOTHERAPY FOLLOWING SYSTEMATIC LYMPHADENECTOMY IN ENDOMETRIAL CANCER: A SINGLE INSTITUTION ANALYSIS

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Aims: The purpose of this study was to evaluate the efficacy and toxicity of systematic lymphadenectomy and postoperative radiotherapy (PORT) in the treatment of endometrial cancer (EC).

Methods: A total of 256 patients with EC between 2000 and 2008 were retrospectively analyzed. Surgery included systematic pelvic and aortic lymphadenectomy, whereas pelvic lymphadenectomy alone was performed to preoperative stage I patients with superficial myometrial invasion and G1 endometrioid adenocarcinoma. PORT was administered to 67 patients with positive lymph nodes, deep myometrial invasion, or adnexal/peritoneal metastases. Prior to PORT, 37 patients with adnexal/peritoneal involvement or aortic node metastases were treated with chemotherapy.

Results: Surgery was undergone in 247 patients, including with 215 pelvic lymphadenectomy and 126 aortic lymphadenectomy. Five-year survival was 97.0% for stage I, 83.3% for stage II, 84.1% for stage III, and 45.2% for stage IV. In PORT group, 13 (19%) were recurred including one (1.5%) intrapelvic recurrence, and five-year survival was 96.7% for intermediate-risk group and 85.3% for high-risk group. Among the patients who had received lymphadenectomy, 19 (8.8%) experienced severe (more than grade 3) ileus and 18 (8.4%) developed severe lymphocystitis. The frequency of severe ileus in PORT group was significantly higher than that in non-PORT group (14/65 vs. 5/150, P< 0.0001). The rates of adverse effects were irrespective of aortic lymphadenectomy.

Conclusions: Surgery with systematic lymphadenectomy followed by PORT was associated with good prognosis but increased rates of ileus in patients with EC. PORT subsequent to lymphadenectomy should limit to relatively high-risk patients.
Poster Session III

PROGNOSTIC SIGNIFICANCE OF GRADE OF LYMPHOVASCULAR SPACE INVASION IN UTERINE SEROUS CARCINOMA

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Objective: The goal of this study was to determine the prognostic value of the grade of lymphovascular space invasion (LVSI) in uterine serous carcinoma.

Patients and methods: Twenty-six patients diagnosed with uterine serous carcinoma between 2001 and 2011 were included. LVSI was classified as absent, mild (1-2 foci), moderate (3-8 foci), or severe (>9 foci). Statistical analysis was performed using Fisher’s exact test, Kaplan-Meier survival curves and Cox proportional hazards model to control for age, stage of the disease and complete or incomplete staging.

Results: The median age was 63.3 years (range 58.6 - 70). The median follow up time was 16.9 months (range 0.6 - 73). LVSI was present in 18 cases (69.2%): mild in 7 (26.9%), moderate in 4 (15.4%) and severe in 7 (26.9%) cases. There was no association between LVSI and pelvic, para-aortic lymph node involvement, ovarian, cervical or distant metastasis. The median disease-free survival with absent or present LVSI was 58 and 49 months, respectively (p>0.05), and the median overall survival with absent or present LVSI was 75 and 55 months, respectively (p>0.05). Disease-free survival was significantly longer in cases of absent LVSI, (median 58 months) and mild LVSI, (median 49 months) than in cases of severe LVSI (median 18 months) (p< 0.05). Overall survival was also significantly longer in cases of absent LVSI (median 75 months) and mild LVSI (median 62 months) than severe LVSI, (median 15.9 months) (p< 0.05).

Conclusions: Severe grade of LVSI is associated with shorter disease-free time and overall survival.
Poster Session III

THE USE OF ADJUVANT CARBOPLATIN AND DOSE-DENSE PACLITAXEL CHEMOTHERAPY FOR THE TREATMENT OF UTERINE PAPILLARY SEROUS CARCINOMA

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Objective: To determine the tolerance and efficacy of traditional q 3-weekly chemotherapy regimen compared to a dose-dense (weekly) regimen in the treatment of uterine papillary serous carcinoma (UPSC).

Methods: UPSC is histologically and clinically similar to serous ovarian carcinoma. It has an aggressive clinical course and is often diagnosed in advanced stage. Evidence is emerging that supports the use of carboplatin and dose-dense paclitaxel chemotherapy in serous ovarian carcinomas. Patients with UPSC at the Tom Baker Cancer Centre (TBCC) who require chemotherapy are now offered this regimen. A retrospective review of all patients diagnosed with UPSC at the TBCC in Calgary, Alberta was performed between 2009 and 2011.

Results: UPSC patients who received the traditional regimen (group A) were compared to those who received the dose-dense regimen (group B). During this time, 43 patients with UPSC were diagnosed. Twenty-six of those were either excluded from analysis (8) or did not receive adjuvant chemotherapy (18). Twelve were in group A, and 5 in group B, corresponding to 72 and 29 chemotherapy cycles, respectively. Most patients completed their regimen, however there were 11 delays in group A and 1 in group B (p=0.13). Most of these were due to hematologic toxicities.

Conclusion: Dose dense chemotherapy for UPSC is well tolerated and has low rate of chemotherapeutic delay. Our standard use of G-CSF in the dose-dense protocol may assist in this regard. Pending recurrence and survival data will shed light on the potential benefits of this new protocol compared with the traditional regimen.
Poster Session III

ARE PREOPERATIVE TUMOR MARKERS USEFUL IN PREDICTION OF POSTOPERATIVE HISTOPATHOLOGICAL PARAMETERS IN ENDOMETRIAL CANCER?

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Aims: To determine if preoperative serum CA125, CA15-3, CA19-9, AFP and CEA levels have an association with postoperative histopathological parameters in terms of tumor histology, grade, tumor size, cervical involvement, depth of myometrial invasion, lymphovascular involvement (LVSI), lymph node metastasis (LNM), positive peritoneal cytology, and peritoneal tumor involvement.

Methods: Data of 130 endometrial cancer (EC) cases treated between January 2008-January 2011 were retrospectively analyzed. Mann-Whitney U, one-way ANOVA tests and ROC curve analysis were utilized to determine the association between tumor markers and histopathological parameters.

Results: Levels of serum CA-125 and CA15-3 were associated with tumor histology, being significantly higher in non-endometrioid tumors (p=0.008). CA-125 levels were significantly higher in cases with LNM (p=0.001), positive peritoneal cytology (p=0.003) and peritoneal tumor involvement (p=0.03). CA-125 >80U/ml was highly predictive (sensitivity 75%, specificity 99%) for peritoneal tumor involvement (p=0.03). Serum tumor marker levels did not have a significant association with tumor size, depth of myometrial invasion, LVSI and cervical involvement (p>0.05).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Optimal CA125 cut-off (U/ml)</th>
<th>AUC</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>P</th>
</tr>
</thead>
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<tr>
<td>Myometrial invasion &gt;1/2</td>
<td>15.5</td>
<td>0.651</td>
<td>66</td>
<td>64</td>
<td>0.01</td>
</tr>
<tr>
<td>Paraaortic LNM</td>
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<td>0.758</td>
<td>64</td>
<td>74</td>
<td>0.002</td>
</tr>
<tr>
<td>Positive cytology</td>
<td>44</td>
<td>0.781</td>
<td>60</td>
<td>90</td>
<td>0.003</td>
</tr>
<tr>
<td>Peritoneal tumor involvement</td>
<td>80</td>
<td>0.807</td>
<td>75</td>
<td>99</td>
<td>0.03</td>
</tr>
</tbody>
</table>

[Table-1]

Conclusions: Preoperative prediction of histopathological factors indicating poor prognosis in EC is important for preoperative patient counselling, estimating the extent of the surgical procedure and anticipating adjuvant treatment. In this study, elevated levels of serum CA125 had a significant association with LNM, which is one of the most important prognostic variables. CA125 levels were also higher in non-endometrioid tumors, which generally have an unfavorable prognosis. Future studies assessing various serum markers and imaging techniques are needed to define an optimal test to preoperatively predict prognostic factors in EC.
Poster Session III

TO ASSESS IMPACT OF REVISED FIGO STAGING ON SURVIVAL OF PATIENTS WITH UTERINE LEIOMYOSARCOMA - SINGLE CENTRE EXPERIENCE

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Objective: To assess whether the 2009 revised International Federation of Gynaecology and Obstetrics (FIGO) staging for uterine leiomyosarcomas has had any impact on overall survival (OS) of our patients, and whether we need to review our current adjuvant treatment strategies.

Method: Retrospective data collected to assess 2 year OS and 5 year OS. Primary treatment had to be a Hysterectomy and Bilateral Salpingo-oophorectomy.

Results: Twelve patients had complete records. 6/12(50%) were poorly differentiated, with 4/6 receiving post-op adjuvant treatment; 2/12(17%) were moderately differentiated, with one receiving adjuvant treatment; 4/12(33%) were well differentiated and none received adjuvant treatment. When patients were staged using old versus new FIGO staging, results were as follows. Stage 1: 7/12(58%) v 8/12(67%); stage 2: 1/12(8%) v 1/12(8%); stage 3: 2/12(17%) v 1/12(8%); and 2/12(17%) v 2/12(17%) had stage 4, respectively. Overall, 5 patients were down-staged (3 in stage 1 from 1B to 1A), one each in stage 2 (2B to 1B) and stage 3 (3A to 2B); none were up-staged. Two year and 5 year overall survival was 67% and 44%, respectively. Five year overall survival by stage (old v new) was 11% v 22% for stage 1; 11% v 11% for stage 2; 11% v none for stage 3; 11% v 11% for stage 4, respectively.

Conclusion: The biggest change noted was 'down-staging' of disease. We did not feel there was significant change in overall survival, and will therefore continue current practise. Overall prognosis remains poor and further clinical studies in this field are needed.
Poster Session III

ANEMIA AND POOR PROGNOSTIC FACTORS IN ENDOMETRIAL CANCER

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Objective: This study aimed to evaluate the relationship between pretreatment hemoglobin and prognostic factors in patients with endometrial cancer.

Methods: Medical records of 228 patients with endometrial cancer who had undergone surgery were retrospectively reviewed. Hemoglobin level in each patient was determined 24-48 hours before the surgery. Association between clinicopathological variables and pretreatment Hemoglobin levels were described using Pearson's chi square test (or two-tailed Fisher's exact test when appropriate). Survival analysis was performed with Kaplan-Meier estimates. Univariate and cox-regression models were used to evaluate the prognostic impact of various factors including hemoglobin levels in terms of disease-free survival.

Results: The median duration of follow-up was 38.2 months. Eighty-nine patients (39%) had a preoperative hemoglobin level of < 12 g/dL. These 89 patients had significant higher rates of nonendometrioid histology, advanced FIGO stage, lymphovascular invasion, cervical involvement, adnexal involvement, positive peritoneal cytology, and lymph node involvement than patients with hemoglobin ≥12 g/dL. The 5-year disease-free survival rate of patients with anemia was 77% compared with 88% for those with hemoglobin ≥12 g/dL (p=0.044). In the multivariate analysis only histology, myometrial invasion, and lymphovascular invasion were proved to be independent prognostic factors whereas tumor grading, stage, cervical involvement, adnexal involvement, positive peritoneal cytology, lymph node involvement, and low hemoglobin were not.

Conclusion: Presence of anemia before treatment may reflect poor prognostic factors in patients with endometrial cancer. Low pretreatment hemoglobin level may have a prognostic impact on disease-free survival.
Poster Session III

ULTRA-LATE PRESENTATION OF RECURRENT GYNAECOLOGICAL CANCER - 30 YEARS FOLLOWING PRIMARY TREATMENT

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Introduction: Most cases of recurrent gynaecological cancer occur within 3 years of primary treatment. We present two patients with such recurrence after more than 30 years.

Case 1: A 76 year old woman diagnosed with endometrial carcinomas in 1981 underwent a total abdominal hysterectomy and bilateral salpingoophorectomy. There was no adjuvant treatment. She subsequently presented with rectal bleeding in 2011.

An annular tumour of the mid sigmoid was found and treated with a sigmoid colectomy. Histology revealed an endometrial adenocarcinoma comparable with the previous specimen from 1981 with positive mesocolic nodes. Adjuvant therapy with provera was commenced.

Case 2: A 68 year old woman presented with pelvic discomfort and a swollen leg 36 years after a total hysterectomy for recurrent CIN 3/occult CA. Clinical examination and imaging revealed a pelvic mass and inguinal lymphadenopathy. Lymph node biopsy confirmed squamous cell carcinoma. She was subsequently treated with chemo-radiotherapy.

Discussion: Regardless of treatment modalities in endometrial and cervical cancer, median time to recurrence is short and 75% occur within 3 years of treatment. The reported 5 year survival rates of patients with recurrence are between 3% to 13%. Advanced or recurrent disease can present a difficult management problem and depends upon the extent of disease, primary treatment and co-morbidities. There are 4 reported cases of recurrence of endometrial cancer after more than 10 years of treatment but none have been reported in the colon.

Recurrences of carcinoma of the cervix presenting as lymphadenopathy have been described before but this is the first time 30 years after treatment.
Poster Session III

RETROPERITONEAL LEIOMYOSARCOMA: PRESENTATION OF A CASE AND A LITERATURE REVIEW

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Introduction: Soft tissue sarcomas constitute 0.7% of adult malignancies. Ten to 20% of soft tissue sarcomas occur in the retroperitoneum. The most common histologic types are leiomyosarcoma, liposarcoma, and fibrosarcoma. The retroperitoneum provides a widely expansible anatomic location for tumors, and these tumors often attain a large size before symptoms are manifest. A diagnosis of retroperitoneal tumor should be considered in patients with unusual pelvic symptoms and physical findings.

Case presentation: A 33-year-old white woman presented to our center after a routine ultrasound examination. The abdominal ultrasound revealed a large mass with solid components arising from the region of the left ovary. Preoperative evaluation consisted of a transvaginal ultrasonography and MRI. Transvaginal ultrasonography confirmed the presence of a solid mass in the anatomical position of the left ovary and MRI examination revealed a pelvic mass possibly origin from the uterus. CEA, AFP, CA 15-3 and CA 125 revealed no signs of malignancy, except from CA 19-9. The patient underwent exploratory laparotomy. The histological examination revealed leiomyosarcoma.

Discussion: Leiomyosarcomas are rare tumors that may arise from any smooth muscle tissue. Physicians often do not think the possibility of retroperitoneal mass. The perioperative diagnosis can be misled by the absence of specific symptoms and the common occurrence of gynecologic tumors. Imaging examinations might help the physician to differentiate possible retroperitoneal masses. In several cases the final diagnosis can not be estimated and the essential for the patient is to be operated. The final diagnosis will be established only after exploratory laparotomy.
Poster Session III

LONG-TERM OUTCOMES AND PROGNOSTIC DETERMINANTS IN WOMEN WITH UTERINE SARCOMA: A SINGLE INSTITUTIONAL EXPERIENCE

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Introduction: Uterine sarcoma is a rare type of uterine cancer.

Objectives: To evaluate the treatment related outcomes and prognostic factors in women with uterine sarcoma.

Methods: We retrospectively studied 81 consecutive cases of women with surgically treated uterine sarcoma at our institution. All histopathologic and clinical data were reviewed.

Results: The median age was 51 years (range 22-93). Thirty-three (40.7%) patients had a carcinosarcoma (CS), 29 (35.8%) had a leiomyosarcoma (LMS), and 19 (23.5%) had an endometrial stromal sarcoma (ESS). According to 1988 FIGO classification, Stage I-II, and III-IV tumors were identified in 50 (61.7%) and 31 (38.3%) patients, respectively. Patients with stages I-II had a recurrent rate of 20% compared to 48.4% of those with stages III-IV (P=0.007). Local, distant, and both recurrences were found in 11 (13.6%), 9 (11.1%), and 5 (6.2%) patients, respectively. The recurrence was found in 14/29 (48.3%) of LMS group, 7/33 (21.2%) of CS group, and 4/19 (21.1%) of ESS group (P=0.04). At a median follow-up of 23 months, overall 5-year survival rates of the patients with ESS, CS, and LMS were 73% (95%CI= 49 to 96%), 31% (95%CI=13 to 50%), and 14% (95%CI= -13 to 41%), respectively (P=0.05). In multivariate analysis, FIGO stage was the only predictor for recurrence (P=0.01). Furthermore, histological type (P=0.038), FIGO stage (P=0.001), and patients' age (P=0.039) were significant predictors for overall survival, respectively.

Conclusions: Recurrences remain a major problem of patients with uterine sarcoma. In comparison to ESS and CS, patients with LMS tend to have a worse prognosis.
Poster Session III

EXPRESSION AND FUNCTIONS OF MEMBRANE-BOUND MUCIN MUC20 IN ENDOMETRIAL CANCER

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Purpose: MUC20 is a transmembrane mucin and the MUC20 mRNA has been detected in various organs. However, its role in tumor malignancy is still unknown. In the present study, the expression and functions of MUC20 were analyzed to elucidate its clinicopathologic significance and potential role in endometrial cancer (EC) carcinogenesis.

Experimental design: The relationship between MUC20 expression and clinical characteristics of EC was analyzed in 97 EC specimens (including 66 endometrioid, 18 serous, 8 clear cell, and 5 mucinous) and 16 normal endometrial tissues by immunohistochemistry. The effects of MUC20 on cell proliferation and tumorigenesis were examined both in vitro and in vivo, using MTT assay, migration assay, invasion assay, and tumorigenesis in SCID mice.

Results: The expression of MUC20 was significantly ($P < 0.005$) higher in cancer samples compared with the normal endometrial tissues. Increased expression of MUC20 in EC tumors correlated with an unfavorable histologic profile ($P < 0.05$) and was a poor prognostic factor for survival as evaluated by univariate and multivariate analyses ($P < 0.005$). Overexpression of MUC20 in EC cell lines significantly enhanced cell proliferation, motility and tumorigenesis.

Conclusion: Our findings suggest that MUC20 protein, as a valuable marker of EC prognosis, plays an important role in the development and progression of human EC.
Poster Session III

A GENE EXPRESSION PROFILE AS A PREDICTOR OF RECURRENCE IN LOW AND INTERMEDIATE-RISK ENDOMETRIAL CANCER

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Aims: Endometrial cancers (ECs) classified as low, intermediate and high-risk based on clinical and pathological features (CPF) are associated with 5%, 15% and 25% risk of recurrence. We examined whether gene expression profile can more accurately predict the prognosis of ECs excluding high risk group of CPF.

Methods: Tumor specimens were obtained from 136 ECs (low/intermediate risk: 67/69), 14 who had recurred and 122 who had not recurred with a median follow-up of 1830 days. Gene expression profiles were performed using the custom array based on our previous report. We established the gene scoring model (GSM) by logistic regression model in 68 cases, and in other 68 test cases, we calculated the recurrent score (RS) based on the GSM.

Results: The area under the curve of receiver operatorating characteristic curve to predict the recurrence based on the GSM was 0.87 in 68 test cases. The sensitivity and specificity of CPF was 86% and 48%. GSM achieved 86% of sensitivity and 67% of specificity based on RS=0.062. Progression free survival (PFS) is significantly longer in patients with RS≤0.062 than that in patients with RS>0.062 (p=0.006), however, CPF was not related with PFS (p=0.09).

Conclusions: GSM can more precisely predict the prognosis of ECs (low and intermediate-risk) than CPF.
Poster Session III

ATTITUDES AND PRACTICES OF KOREAN GYNECOLOGISTS CONCERNING HORMONE REPLACEMENT THERAPY IN ENDOMETRIAL CANCER SURVIVORS

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Objectives: To investigate the prescribing patterns of Korean gynecologists with regards to hormone replacement therapy (HRT) after endometrial cancer treatment.

Material and methods: A questionnaire was distributed to 163 Korean gynecologists. The questionnaire addressed the attitudes and the treatment strategies regarding HRT for patients who had been previously treated for endometrial cancer.

Results: Of the 163 gynecologists who were sent the questionnaire, 98 (60.1%) responded. Among the respondents, 82.7% had previous experience prescribing HRT to patients with endometrial cancer. Among the respondents who had administered HRT, 92.6% had prescribed HRT to patients with Stage I endometrial cancer and more than half of them had also prescribed HRT to Stage II. Among the respondents who had administered HRT, 40.7% had prescribed HRT without regard to cancer-cell type and 40.7% started HRT from 2 years after endometrial cancer treatment. Tibolone was the most commonly prescribed drug (61.9%). The most common reason not to choose is the fear of recurrence (38.1%).

Conclusion: In conclusion, most of the Korean gynecologists had experience in prescribing HRT to endometrial cancer patients. Although HRT is not actively recommended, HRT given post-therapy to endometrial cancer patients is considered to be a relatively acceptable form of therapy by them.
Poster Session III

HE4 - A NOVEL PROGNOSTIC FACTOR IN ENDOMETRIAL CANCER?

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**Background and aim:** New technologies and methods are urgently needed for the diagnosis of endometrial cancer in early stages. HE-4 is one of WAP proteins. An accurate biomarker for EC might provide a preoperative prognostic value to predict the scope of surgical staging. The aim of this prospective pilot study is to investigate a possible correlation of HE-4 and Ca 125 with tumour differentiation and depth of the invasion into the myometrium.

**Methods:** All women were postmenopausal, average age 66. The blood samples obtained of 40 women with EC confirmed pre-operatively the presence of HE4 and Ca 125. The serum levels of HE4 were determined using Abbott Architect assay. All women subsequently underwent surgery. Histological type, depth of myometrial invasion, grading and stage of disease were recorded after histological examination of the tumour.

**Results:** Invasion depth in myometrium up to half (N=27), median HE-4 (range): 56.1 (16.6; 123.8), more than half (N=13), median HE-4 (range): 113.7 (38.0; 992.5), p = 0.001.

Serum He-4 levels ≥ 80 pmol/L displayed a sensitivity of 84.6% and a specificity of 77.8% in identifying stage IA versus IB.

**Conclusions:** Our preliminary results indicate possible correlation between HE-4 levels and depth of myometrial invasion and support the hypothesis where HE4 is a useful marker in the preoperative staging of endometrial cancer as well as it is an important factor in prediction of the planned surgery scope. Our results do not support the idea of correlation between Ca 125 levels and depth of myometrial invasion.
Poster Session III

ISOLATED CUTANEOUS METASTASIS OF UTERINE LEIOMYOSARCOMA: CASE REPORT AND REVIEW OF LITERATURE

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A 54 year old lady was referred to the surgical day ward for routine excision of a scalp lesion thought clinically to represent a sebaceous cyst of the right occiput. She had presented 4 years earlier with menorrhagia, fatigue and iron-deficiency anaemia and was diagnosed with a fibroid uterus on ultrasound examination after inconclusive diagnostic laparoscopy. She underwent total abdominal hysterectomy and right salpingo-oophorectomy for 3 large uterine fibroids. Histopathological examination of the hysterectomy specimen revealed an incidental low-grade leiomyosarcoma. Staging CT thorax, abdomen and pelvis (TAP) was negative for metastatic disease. She was treated further by adjuvant pelvic radiotherapy. Clinical and radiological follow up showed no objective evidence of metastatic.

She noticed an uncomfortable cystic swelling on her occiput four years after hysterectomy and was referred for routine excision of what was believed to be a benign lesion. The lesion was excised and sent for histopathological examination. Microscopic analysis including immuno-histochemistry demonstrated an ER and PR positive metastatic deposit of leiomyosarcoma. The margins of excision were histologically clear of disease.

At Multi-Disciplinary Team (MDT) discussion with input from pathologists, gynaecologists, medical oncologists, radiation oncologists and surgeons, including review of the original hysterectomy slides, a confirmed diagnosis of metastatic scalp deposit from previous uterine leiomyosarcoma was made. Re-staging CT TAP and MRI brain were negative for local recurrence or distant metastases. She is currently undergoing radiotherapy to the scalp and surrounding tissues, and may require salvage adjuvant chemotherapy in the future if other sites of metastatic disease are detected.
Poster Session III

PARAAORTIC LYMPH NODE DISSECTION FOR WOMEN WITH ENDOMETRIAL ADENOCARCINOMA AND INTERMEDIATE TO HIGH-RISK TUMORS: DOES IT RESULT IN IMPROVED SURVIVAL?

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Introduction: Literature suggests that paraaortic lymphadenectomy (PALND) has a therapeutic benefit in addition to providing diagnostic and prognostic information for women with intermediate to high-risk endometrial adenocarcinoma. We hypothesized that the observed survival advantage of PALND is a reflection of the general health of the patient rather than a therapeutic benefit of surgery.

Methods: Women with intermediate to high-risk endometrial adenocarcinoma diagnosed from 2002-2010 at a single institution were identified. Medical comorbidities and disease details were abstracted. Chi-square or t-test was used for all univariate analysis. Overall survival (OS) and disease specific survival (DSS) were calculated using the Kaplan-Meier method and compared using the log-rank test.

Results: A total of 253 women were identified. Of these, 174 had pelvic lymphadenectomy (PLND) and 82 had PALND. The rate of positive nodes was 13% for women with PLND and 7% for women with PALND. Patients who had PALND had a lower BMI (31 v. 35, p=0.013) and a smaller proportion had diabetes (16% v. 30%, p=0.02), hypertension (46% v. 61%, p=0.03), pulmonary disease (4% v. 15%, p=0.009) or coronary artery disease (1% v. 9%, p=0.02). Five-year OS was improved in patients who had PALND (96% v. 82%, p=0.007). However, there was no difference in 5-year DSS (96% v. 89%, p=NS).

Conclusions: Women with intermediate to high-risk endometrial adenocarcinoma who undergo PALND have improved OS but no improvement in DSS. The improved OS may be a function of superior underlying health status as opposed to a therapeutic benefit of lymphadenectomy.
Poster Session III

TRANS CERVICAL RESECTION OF THE ENDOMETRIUM TO TREAT EARLY ENDOMETRIAL CANCER IN MORBIDLY OBESE, HIGH SURGICAL RISK PATIENTS

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Introduction: Obesity is now endemic in today’s society and surgical techniques have to adapt to the changing shape of the population. The morbidly obese patient with endometrial cancer provides a particular challenge. The pathogenetic factors of this disease ensure that often these patients have a myriad of serious co-morbidities making these patients highly unsuitable surgical candidates.

Objective: To demonstrate the safe and successful use of trans cervical resection of the endometrium (TCRE) to treat early endometrial disease (1a) in women with extremes of BMI in the cancer centre in Northern Ireland.

Methods: Case series analysis of 6 patients all deemed unsuitable or extremely high risk for more aggressive surgery due to presence of extensive co-morbidities including very high BMI.

We demonstrate the technique with high quality video footage demonstrating the three layer resection technique stripping tissue down to the myometrium. Each layer undergoes histological examination to assess extent of disease. A Mirena IUS is inserted following resection. Patients are then reviewed every six months initially. Results: All patients had BMIs ranging from 47-67. Median survival is 36 months to date. All avoided general anaesthetic and were treated under spinal. There were no complications. All patients are subject to long term follow by Local Anaesthetic hysteroscopy. There has been biopsy proven successful resection of endometrial cancer.

Conclusion: TCRE is a safe and feasible technique for the management of endometrial cancer in poor surgical candidates with morbid obesity.
Poster Session III

WOMEN WITH PAPILLARY SEROUS UTERINE CARCINOMA; AN EVALUATION OF THERAPY

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Background and aims: Endometrial carcinoma is the most common gynaecologic malignancy in the Western world. Most cases present with early stage disease and prognosis is good. Uterine papillary serous carcinoma (UPSC) is a histological variant of endometrial cancer which is found in 10% of women with endometrial cancer. However this histopathological subtype is responsible for 40% of the deaths due to endometrial cancer. We investigated prognostic outcomes of different treatment options to improve guidelines for UPSC.

Methods: This retrospective cohort study includes women treated for UPSC between 1990 and 2011 in the three hospitals connected to the Centre of Gynaecologic Oncology Amsterdam. Data were collected from medical files and analyzed in SPSS statistics software. Until now 56 women from one hospital are included in this study.

Results: Mean follow-up was 2.16 years (range 0.08-15.91). In 17 patients staging surgery was performed. Preliminary results show that 47% (n=8) of UPSC patients have positive lymph nodes at the time of staging. While only 12.5% (n=1) with positive lymph nodes showed any signs of lymphadenopathy on CT or MRI. Unstaged patients (n=17) were more likely to receive radiotherapy compared with patients who were staged with negative lymph nodes. 41% of the staged patients underwent secondary surgery to ensure complete staging. At this moment no significant differences in survival were seen between staged and unstaged patients.

Conclusion: These preliminary results prove that UPSC is an aggressive variant of endometrial cancer with early spread beyond the uterus. Staging surgery results in tailored therapy, less radiotherapy.
Poster Session III

RISK OF RECURRENCE IN STAGE III, HIGH- GRADE ENDOMETRIAL CANCER (HEC), BY PRIMARY TUMOR FACTORS (PTF) AND TREATMENT RECEIVED

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Background: The implications of surgical and pathologic findings in stage III, HEC are controversial. This study sought to determine the contribution of PTF versus treatment (TT) received (chemotherapy (CT) or radiation (RT)) in recurrence and survival outcomes.

Design: A retrospective cohort study was performed, including all patients with surgical stage III HEC at our institution (1999 - 2009). PTF such as stage, histologic subtype, grade, lymphovascular invasion (LVS), extent of myometrial (MI) and cervical invasion (CI), serosal (SI) and adnexal involvement (AI), parametrial (PI) and vaginal (VI) involvement, nodal status and margins (MR) were assessed. Hazard ratios were determined using Cox Proportional Hazards modeling.

Results: There were 82 patients (mean age = 66 ± 11 years) with stage III HEC (IIIA - 38%, IIIB - 7%, IIIC - 55%). Median follow-up was 22 months and median time to recurrence was 8.5 months. In univariate analyses, recurrence was associated with SI (p = 0.04), positive MR (p = 0.0003), CI (p = 0.001) and histology (p = 0.01). When controlling for PTF and TT received, clear cell and carcinosarcoma histologic subtypes (HR 8.6 and 6.0, respectively) as well as cervical stromal invasion (HR 3.7) were associated with increased risk of recurrence. Patients who received CT or RT experienced decreased risk of recurrence (HR 0.42 and 0.48, respectively).

Conclusion: When controlling for PTF and TT received, PTF such as histologic subtype and cervical stromal invasion are associated with risk of recurrence, while adjuvant treatment with CT and/or RT may decrease risk.
Poster Session III

LONG-TERM TRENDS IN THE SURVIVAL OF UTERINE CANCER PATIENTS IN CANADA: A POPULATION-BASED STUDY

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Introduction: Annually in Canada, uterine cancer affects approximately 4500 women and 790 are expected to die of their disease. To better understand survival trends across the country we undertook this population based study of Canadian women diagnosed with uterine cancer. Long term trends in relative survival were evaluated by age and geographic region of residence.

Methods: Women with an ICD-10 code of C54 and invasive endometrioid tumours were identified from the Ontario Cancer Registry. They were included if the incident diagnosis occurred between 1992 and 2005, and they were 16 years and older at diagnosis. A flexible parametric model was used to determine relative survival ratio (i.e., the observed survival rate among cancer patients divided by the expected survival rate in the general population).

Results: 18,486 women were diagnosed with uterine cancer. Mean age was 63.4 (SD=11.8) year. Relative survival decreased with each successive age group cohort of patient. When relative survival was adjusted for age, women in British Columbia had the best outcomes. Five-year survival outcomes improved for each age group cohort during the 1992 to 2005 time frame.

Conclusions: Regional variations in relative survival were identified across Canada for women with uterine cancer. This suggests that other factors related to the patient or processes of care are involved. Examining these factors in further detail may provide opportunities to improve the care of women with uterine cancer in Canada.
Poster Session III

LONG-TERM CLINICAL OUTCOME AND PATTERN OF RECURRENCE OF 850 PATIENTS WITH STAGES I-II ENDOMETRIAL CARCINOMA. A SINGLE INSTITUTION EXPERIENCE

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Objectives: To study the different predictors of outcome and pattern of loco-regional recurrences for patients with endometrioid carcinoma 2009 FIGO stages I-II.

Methods: Our uterine cancer database with 1450 patients was reviewed. We identified 850 consecutive patients with endometrioid adenocarcinoma, stages I-II who underwent hysterectomy between 1989 and 2010. Patients with non-endometrioid carcinoma, mixed histology were excluded. The recurrence rate was estimated using Kaplan-Meier approach from the date of hysterectomy. The Cox regression was used to explore the risks of various factors on recurrence.

Results: Median follow-up was 5.6 years. Median age was 63 years. 27% were African American. All patients underwent TAH-BSO with and without lymph node dissection. Peritoneal cytology was performed in 81%. 31% of patients received adjuvant RT (with vaginal cuff brachytherapy (VB) alone, pelvic external beam (EBRT), or both). Recurrence-free survival at 5 and 10 year were 94% and 93%, respectively. Median time to recurrence was 1.2 years (range, 0.4-8.7). The site of recurrence was mainly vaginal (74%) for those who did not receive adjuvant RT. On multivariate analysis, the following factors were statistically significant independent predictors of recurrences; grade 3 tumors (p=< 0.001), stage II (p=< 0.001), non utilization of adjuvant RT (p=< 0.001), African American race (p=< 0.030) and age older than 65 (p=0.045).

Conclusion: In this large series of patients with FIGO stages I-II endometrioid adenocarcinoma, grade 3, higher FIGO stage, African American race, non utilization of adjuvant radiation treatment and older age were independent significant predictors of tumor recurrence.
Poster Session III

CD133+ CANCER STEM CELLS DERIVED FROM UTERINE CARCINOSARCOMA (MALIGNANT MIXED MÜLLERIAN TUMOR)

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Cancer stem cells (CSCs) that display tumor-initiating properties have recently been identified. CD133, a surface glycoprotein linked to organ-specific stem cells, has been described as a marker of CSCs in different tumor types. We herein identify and characterize CSCs in human uterine carcinosarcoma (malignant mixed Müllerian tumor), which is one of the most aggressive and therapy-resistant gynecological malignancies and is considered to be of mesodermal origin. The CD133+ population was increased in uterine carcinosarcoma, and this population showed biphasic properties in the primary tumor. CD133+ cells predominantly formed spheres in culture and were able to differentiate into mesenchymal lineages. CD133+ cells were more resistant to cisplatin/paclitaxel-induced cytotoxicity in comparison with CD133- cells. A real-time polymerase chain reaction analysis of the genes implicated in stem cell maintenance revealed that CD133+ cells express significantly higher levels of Oct4, Nanog, Sox2, and Bmi1 than CD133- cells. Moreover, CD133+ cells showed a high expression level of Pax2 and Wnt4, which are genes essential for Müllerian duct formation. These CD133+ cells form serially transplantable tumors in vivo and the resulting CD133+ tumors replicated the EpCAM, vimentin, and estrogen and progesterone receptor expression of the parent tumor, indicating that CSCs likely differentiated into cells comprising the uterine carcinosarcoma tissue. Moreover, strong CD133 expression in both epithelial and mesenchymal elements in primary tumor demonstrated significant prognostic value. These findings suggest that CD133+ cells have the characteristics of CSCs and Müllerian mesenchymal progenitors.
MULLERIAN ADENOSARCOMA WITH SARCOMATOUS OVERGROWTH ARISING FROM AN ADENOSARCOMA  
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Mullerian adenosarcomas are rare neoplasms characterized by an intimate admixture of benign epithelial and malignant stromal components. They are generally regarded as tumors having a low malignant potential. When characterized by a focal overgrowth of sarcomatous elements that comprise at least one-fourth of the entire tumor, the behavior becomes entirely different. These neoplasms, termed mullerian adenosarcomas with sarcomatous overgrowth (MASO), were found to exhibit a highly malignant course characterized by local recurrences, metastases, and death. A rare case of MASO, the third of its kind to be reported in the Philippines, is herein presented.  

A 34-year old nulligravid who underwent myomectomy for adenomyoma presented with abdominal pain, associated with rapid abdominal enlargement, two months after surgery. Laparotomy revealed a 20 x 18 cm solid friable pelvic mass adherent to the omentum, left anterior abdominal wall, lateral abdominal & posterior abdominal walls. Biopsy of the mass revealed mullerian adenosarcoma with sarcomatous overgrowth. Review of the slides during the first surgery revealed adenosarcoma. The appearance of sarcomatous overgrowth in the specimens taken from the second surgery implies that this is probably a case of MASO arising from an adenosarcoma.
Poster Session III

CLINICOPATHOLOGICAL RISK FACTORS FOR PELVIC LYMPH NODE METASTASIS IN CLINICAL EARLY STAGE ENDOMETRIOID ENDOMETRIAL ADENOCARCINOMA

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Aims: To identify the clinicopathological risk factors for pelvic lymph node metastasis (PLNM), and to evaluate the predictive significance of these factors for lymphadenectomy in clinical early stage endometrioid endometrial adenocarcinoma (EEA).

Methods: Six hundred and twenty-one clinical early stage EEA patients (tumor confined to uterus diagnosed pre- or intra-operatively) who underwent hysterectomy + bilateral salpingo-oophorectomy + pelvic and/or para-aortic lymphadenectomy between 1989-2006 in Obstetrics and Gynecology Hospital of Fudan University were retrieved. The predictive value of risk factors for PLNM was analyzed.

Results: The positive PLNM rate was 3.9%. Five-year disease related mortality rate in positive PLNM group was 25%, whereas that in negative group was 0.8%. The positive PLNM rates were higher in patients with higher grade tumor, deep myometrial invasion, cervical stromal involvement and lymphovascular space involvement (LVSI). The sensitivity and specificity of old age (≥60), grade 3, deep myometrial invasion, cervical stromal involvement and LVSI in predicting PLNM were 25.0%, 41.7%, 70.8%, 20.8%, 41.7% and 79.1%, 88.4%, 85.6%, 95.6%, 94.5%, respectively. Multivariate analysis revealed deep myometrial invasion and LVSI were independent risk factors for lymph node metastasis. Combined with these two factors as diagnostic criteria, the negative predictive value and specificity were 97.3% and 89.1%, respectively.

Conclusion: Clinical early stage EEA patients with PLNM had much worse prognosis, though the metastasis rate was low. Deep myometrial invasion and LVSI combination were superior predictive criteria for PLNM. Accurate evaluation of these factors pre- or intra-operatively will be beneficial to predict PLNM and guide the operation.
Poster Session III

ROBOTIC SURGERY COMPARED TO LAPAROTOMY STAGING FOR SEROUS PAPILLARY AND CLEAR CELL ENDOMETRIAL CANCER: OPERATIVE AND EARLY FOLLOW-UP OUTCOMES

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Objective: To compare the operative and short term survival of robotic (R) and open (O) staging of serous papillary(SP) and clear cell(CC) endometrial cancer.

Methods: Operative and short term follow-up data were retrospectively reviewed for staging of SP and CC endometrial cancer performed by two oncology services, one staging the procedures open the other robotically. Staging included TAH, BSO, LND, omentectomy, and appendectomy. Patients from March 2009-April 2011 having pathology confirmed SP or CC were included. Chi square test, t-test, and Fisher’s exact test were used, P< 0.05 was significant.

Results: There were 15 patients in the O arm, 16 in the R arm. Stage at diagnosis for the R and O arms were I (11/16), II (2/16), III (0/16), IV (3/16) vs I (5/15), II (4/15), III (6/15), IV (0/15). There were no operative complications for O and 2 minor complications in R. The R arm had a significantly shorter mean operative time (172.5 vs 113.9 mins, P=0.0001), EBL (65 vs. 310 ml, P=0.0002), hospital stay (1.2 vs 5.4 days, P=0.0017) and decreased number of extracted pelvic lymph nodes (11 vs 17.5 nodes, P=0.0080 ). Six month survival data was similar [NED: 9 (56%) vs 7(46%) P=0.226; Recurrence 2 (12.5%) vs 2 (13.3 %) P=1.000; Overall survival 12 (75%) vs 9 (60%), P=0.3217; Lost to follow-up 3 (18.8 %) vs 4 (26.7%), P=0.6851] for R vs O respectively.

Conclusions: Robotic staging is safe with decreased EBL, operative time and hospital stay with similar survival to laparotomy at 6 months.
Poster Session III

ROLE OF SURGICAL STAGING AND ADJUVANT TREATMENT IN UTERINE SEROUS CARCINOMA


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Background and aims: This study evaluates the association of clinical and pathologic characteristics of patients with uterine serous carcinoma (USC) with disease recurrence.

Methods: Surgically-staged patients with USC between 2002 and 2008 at a single institution were identified. Exclusion criteria included neoadjuvant chemotherapy and synchronous gynecologic malignancies. Clinical and pathologic variables were compared with standard statistical methods.

Results: Of the 50 patients included for analysis, disease distribution was as follows: 22-stage I, 5-stage II, 16-stage III, and 7-stage IV. Seventy-five percent of patients received adjuvant chemotherapy, 51% received radiation therapy, and 47% received both. After a median follow-up of 33 months, 42% of patients had disease recurrence. On univariate analysis, factors predictive of disease recurrence included stage ($P < 0.001$), LVSI ($P = 0.03$), positive pelvic cytology ($P = 0.05$), extension to serosa ($P = 0.004$), adnexa ($P = 0.001$), omentum ($P < 0.001$) and appendix ($P = 0.03$). On multivariable analysis, positive pelvic lymph nodes were associated with a shorter interval between surgery and recurrence: 13.6 months PFS with positive vs. 17.2 months with negative lymph nodes ($P = 0.05$). Patients with early stage disease who did not receive any adjuvant treatments had a significantly greater risk of disease recurrence (44.4% vs. 7.70%, $P = 0.043$).

Conclusions: In this population of surgically-staged patients with USC, pelvic lymph node metastases were predictive of a shorter PFS. Adjuvant therapy should be considered in patients even with early stage disease. Prospective trials of adjuvant therapies are urgently needed in this patient population.
Poster Session III

VEGF AND VEGFR1 SERUM LEVELS COMPARISON WITH CA125 IN ENDOMETRIAL CANCER PATIENTS

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Background and aims: The purpose of this study was to answer the question, whether the measurement of the pre-treatment VEGF, and VEGFR1 serum levels would be present better sensitivity than a assessed tumor marker CA125 in the diagnosis of endometrial cancer patients, especially in patients with non-advanced stages.

Methods: The study was based on 55 untreated patients with endometrial cancer, and 52 healthy controls. All tumors were verified histologically and staged according to FIGO classification. Concentrations of CA 125 were determined using the Abbott instruments system, VEGF by the ELISA of R&D, and VEGFR1/sFLT1/ by Roche kits. For the statistical analysis Mann-Whitney U tests, receiver-operating characteristic (ROC) curves to assess the diagnostic sensitivity and specificity of the marker results were used.

Results: In endometrial cancer patients, as compared with controls, there were significantly higher serum levels of CA125 (p< 0.0001), VEGF (p< 0.00001), VEGF R1 (p< 0.00004). The elevated levels of VEGF for 56% patients were found. The concentrations of VEGFR1 and CA125 were elevated in 27% and 25% of patients (respectively). In patients with non-advanced stages (FIGO IA-IC) the sensitivity of VEGF (53%) and its receptor 1 (24%) were higher than CA125 (13%). The ROC analysis revealed the highest diagnostic sensitivity of VEGF (AUC 0.875), however AUC of CA125 and VEGFR1 were 0.773 and 0.757. The significance differences between AUCs values were not approved.

Conclusions: The results provides evidence that measurements of circulating VEGF present superior diagnostic sensitivity, especially in the patients with non-advanced endometrial cancer.
Poster Session III

INCIDENCE OF OVARIAN METASTASES IN UTERINE LEIOMYOSARCOMA AND OPTIMAL SURGERY

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Background: Uterine leiomyosarcoma (LMS) is a rare malignant tumor of uterus. The main method of treatment of LMS is surgery. The efficacy of chemotherapy and radiotherapy is questionable. The aim of our study is to establish the incidence of ovarian metastases and the optimal extent of surgery for uterine leiomyosarcoma in patients of different age groups.

Methods: A retrospective chart review was done to 198 patients with LMS treated at the N.N. Blokhin Russian Cancer Research Center, Moscow, Russia from 1970 to 2009. Patients with LMS had a median age of diagnosis 48.16±0.7 years. Surgical treatment, as independent method, was performed to 126 patients (63.6 %). Combined treatment, including surgery+postoperative chemotherapy or surgery+ radiotherapy was performed to 60 patients (30.3 %). Complex treatment (surgery + chemotherapy + radiotherapy) was performed to 13 (6.5 %) patients.

Results: We observed association between ovarian preservation and improved survival: overall 5 year survival in patients with ovarian preservation and those who underwent oophorectomy is 87.3 ± 8.4 % and 49.0 ± 5.3 %, respectively (p< 0.05). We didn't observe metastases in ovaries in any of 198 patients included in this study. Furthermore, we observed that in radically treated patients the frequency of distant metastases was 22.2% higher in patients with ovaries removed compared to patients with ovarian preservation during the primary surgery(59.7% and 37.5% respectively) (p< 0.05).

Conclusion: According to our data, the optimal surgery for LMS is total abdominal hysterectomy in the reproductive age and total abdominal hysterectomy with bilateral salpingo oophorectomy in the postmenopausal period.
**Poster Session III**

**PROGNOSTIC IMPACT OF LYMPH VASCULAR SPACE INVASION IN EARLY STAGE ENDOMETRIAL CANCER**

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**Background:** Treatment of early stage endometrial cancer consists of hysterectomy and bilateral salpingoophorectomy. Adjuvant radiotherapy is recommended when ≥2/3 risk factors stated by the PORTEC trial are present: age >60, grade 3 and ≥50% myometrium invasion. The PORTEC-II study demonstrated that vaginal brachytherapy (VBT) was equally effective as external radiotherapy (EBRT) for local control, but with less morbidity. Lymph vascular space invasion (LVSI) is not incorporated in the risk criteria as its impact has not been studied in large groups.

**Methods:** 97 patients diagnosed with LVSI positive, early stage endometrial cancer between January 2005 and December 2011 at the Comprehensive Cancer Center South and January 1999 and December 2009 at the Catharina Wilhelmina Hospital and Radboud University Nijmegen Medical Center were included. Data on tumor characteristics, treatment and outcome were extracted from their file.

**Results:** 30 patients had only 1 of the PORTEC risk factors. 67 of the patients had ≥ 2 risk factors. Adjuvant therapy groups were: observational (n=11), VBT (n=25), EBRT (n=24) and VBT+EBRT (n=7) There was a recurrence rate of 20% after VBT (5/25) and 17% (4/24) after EBRT, the majority at a distant site (7/9). Although numbers are low EBRT seems to reduce the number of regional recurrences but does not affect distant metastasis.

**Conclusion:** The presence of LVSI in early stage endometrial cancer is associated with a risk of distant failures. EBRT instead of VBT could be considered to improve loco-regional control. Whether systemic therapy might protect against distant metastasis should be studied.
Poster Session III

METASTASIS OF MALIGNANT MIXED MULLERIAN TUMOR OF THE UTERUS TO THE RECTUS MUSCLE AND SKIN OF MONS PUBIS

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Introduction: Malignant mixed mullerian tumors (MMMT) of the uterus are rare, invasive neoplasms, and have a high rate of metastasis. They are the most common variety of mixed biphasic epithelial (carcinoma) and non-epithelial (sarcoma) endometrial tumors, with a clinically aggressive course. This tumor spreads locally within the pelvic cavity and distally to the regional lymph nodes, lungs and liver. It metastasizes similar to endometrial carcinoma of the uterus, with recurrence occurring commonly in the upper abdomen with occasional distant spread. Reported metastatic sites are the abdomen, pancreas, liver, lung, thyroid gland, and the eye.

Case report: A 68-year-old postmenopausal woman underwent explorative laparotomy with the diagnosis of MMMT which was established with endometrial sampling. Upon physical examination, a 7x5cm area of tumoral nodules on the mons pubis and a 3 cm left inguinal mass were seen, which were subsequently reported as metastasis of MMMT on pathologic examination after removal during laparotomy (Figure 1). Besides, multiple metastatic nodules were detected over the pelvic and abdominal peritoneum, sigmoid colon, and inside the rectus muscle.

[Figure 1]
Discussion: Our case reveals an unusual sites of MMMT metastasis, which are rectus muscle, skin of mons pubis and inguinal area. To the best of our knowledge, this is the first reported case of these unique metastatic sites.
Poster Session III

CLINICOPATHOLOGIC ANALYSIS OF THE P53 SIGNATURE IN THE ENDOMETRIAL POLYP

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Objectives: Postmenopausal status in women with endometrial polyp has been associated with an increased risk of endometrial malignancy. The p53 signature (p53S) was suggested to be a latent precursor for serous carcinoma. We evaluated clinicopathologic features of p53S in the endometrial polyps.

Methods: The immunostainings of p53, estrogen receptor (ER) and Ki-67 were done in 49 postmenopausal endometrial polyps (post-Ps) and 41 the premenopausal endometrial polyps (pre-Ps). The p53S was defined to show p53 labeling index (LI) of 50% or more. The p53 mutation was analyzed in 5 endometrial polyps. This study was approved by the institutional review board.

Results: The mean ages of women with pre-P and post-P were 40 and 65 years, respectively. The mean diameters of pre-Ps and post-Ps were 1.8cm and 1.7cm, respectively. The p53S was found in 6(12%) of post-Ps, but not in pre-Ps. All polyps including p53S were positive stained for ER. LIs of Ki-67 in pre-P and post-P were 31.4% and 37.8%, respectively. LI of Ki-67 for p53S were low to be compared with that of ki-67 for the surrounding endometrial glands. The positive correlation between LIs of p53 and ki-67 was found in pre-P (r=0.744, P< 0.001), but not in post-P (r=0.364). Missense mutation (codon 165:ATG - ATA) was shown in 1 of 3 post-Ps with p53S.

Conclusion: The proliferative activity of post-P showed no significant difference from that of pre-P. The role of p53 in post-P may be different from that of p53 in pre-P.
Poster Session III

RECURRENCE PATTERN OF ENDOMETRIAL CANCER ACCORDING TO NODAL METASTASIS

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Objective: The purpose of this study is to analyze recurrence pattern depending on pelvic and paraaortic lymph node involvement in endometrial cancer.

Methods: We reviewed medical records of 392 patients with endometrial cancer between Jan 2000 and April 2011.

Results: Among them 328 patients underwent primary surgery with pelvic lymphadenectomy (PLND) and 49 patients with pelvic and paraaortic lymphadenectomy (PALND). Twenty one patients (6.4%) had disease recurrence. Metastatic PLN group had higher recurrence rate than non-metastatic PLN group (19.0% vs 4.6%, respectively; P=0.002). The most common treatment failure site was peritoneum in these two groups (62.5% vs 53.8%, respectively). Metastatic PALN was not a statistically significant factor related with tumor recurrence (P=0.951). Metastatic PALN only with non-metastatic PLN group (n=3) had no treatment failure or recurrence in this study. Stage was an independent predictive factor of treatment failure in non-metastatic PLN group (P< 0.001) not in metastatic PLN group (P=0.141).

Conclusions: In endometrial cancer, metastatic PLN had the more effect on disease recurrence than metastatic PALN.
Poster Session III

DISTRIBUTION OF TH17 CELLS AND TREGS IN TUMOR-INFILTRATING LYMPHOCYTES IN PATIENTS WITH UTERINE CERVICAL CANCER

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Background: Recent studies suggest a potential impact of Th17 cells on tumor. In the present study, we investigated the distribution of Th17 cells in relation to Tregs in the tumor-infiltrating lymphocytes (TILs) of uterine cervical cancer (UCC) patients, cervical tissues of patients with cervical intraepithelial neoplasia (CIN) and healthy cervical tissues.

Methods: Th17 cells and Tregs were evaluated by immunohistochemical staining. IL-6, TGF-β, IL-17 and IL-10 were detected respectively by enzyme-linked immunosorbent assay (ELISA). Moreover, immunohistochemical staining for microvessel density (MVD) were performed in order to assess the association of IL-17 expression with angiogenesis.

Results: Compared with controls, patients with UCC or CIN had a higher proportion of Th17 cells and Tregs, when the ratio of Th17/Treg in TILs was decreased in individual cases, it was more markedly decreased in TILs than normal cervical tissues. Meanwhile, the cytokine (IL-6, TGF-β and IL-10) concentrations were significantly higher in UCC patients than those in healthy controls. Interestingly, the levels of intratumoral Th17 cells were positively correlated with MVD in tumors.

Conclusions: In conclusion, the imbalance of Th17/Treg may play critical roles in the development and progression of UCC and Th17 cells may promote tumor progression through fostering angiogenesis.
Poster Session III

DOUBLE-NEGATIVITY FOR ESTROGEN AND PROGESTERONE RECEPTOR EXPRESSION IS AN INDEPENDENT RISK FACTOR FOR RELAPSE IN ENDOMETRIOID ENDOMETRIAL CANCER PATIENTS

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Background: Estrogen and progesterone receptors have an established role in endometrioid endometrial cancer (EEC) diagnosis. Triple negative phenotype (TNP) is a known poor prognostic factor in breast cancer and possibly in EEC. Our aim was to examine the effect of TNP has on disease relapse.

Methods: We collected clinical and histopathological data on 218 EEC patients operated at Turku University 2004-2007 with a minimum of 3.5 years follow-up. A tissue microarray (TMA) was constructed from the paraffin embedded tissue samples for immunohistochemical analysis and stained for ER, PR and ERBB2 expression. Data was analyzed with χ², logistic regression analysis and Kaplan-Meier analysis.

Results: 23 (10.6%) of EEC patients were diagnosed with a relapse during follow-up. Median disease free time for patients with relapse was 48.6 months. 28 (12.8%) were TNP of which 10 relapsed. In multivariate analysis, when adjusted to FIGO grade and stage the OR for relapse in TNP was $4.54(1.50-13.73)$ $p=0.007$. In patients with negative ER and PR (=double negative) expression $(n= 30)$ the OR was $5.40 (CI 1.75-16.62)$ $p=0.003$ when adjusted for FIGO stage and grade.

Conclusion: Our results indicate that patients with double negative EEC have a similar risk of disease relapse than patients with TNP.
Poster Session III

THE mRNA EXPRESSION OF POLYCOMB GENES AND ITS CLINICOPATHOLOGICAL SIGNIFICANCE IN ENDOMETRIAL CARCINOMA

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Objectives: The Polycomb group (PcG) genes are a class of regulators responsible for maintaining homeotic gene expression. PcG expression is deregulated in various types of human malignancies, however their expressions have not been examined in endometrial cancer. We investigate the expression of members of PcG and their clinicopathological roles in endometrial cancer.

Methods: The expression of EZH2, EED, CBX8, BMI1 and Bmi-1 in a series of 63 endometrioid endometrial carcinoma tissues was assayed by quantitative real time RT-PCR. The correlation between PcG mRNA expression and clinicopathological characteristics were examined. In addition, the correlations of the expression of major cyclins with polycomb genes were examined.

Results: Among PcG genes, mRNA level of EED was significantly correlated to FIGO staging and lymph node metastasis. In addition, mRNA level of EZH2 showed the strong and positive correlation with that of cyclin A2, known indicator of poor prognosis for endometrial cancer.

Conclusions: The results suggested that PcG genes is involved in the progression of endometrial carcinoma and EZH2 is involved in the regulation of cyclin A2 expression in endometrial carcinoma.
Poster Session III

A FOCI OF ENDOMETRIAL RECURRENCE IN A YOUNG PATIENT WITH ENDOMETRIAL CANCER ON THE FERTILITY-SPARING TREATMENT

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Background and aims: A few reports have suggested that young patients with endometrial carcinoma could be treated conservatively and achieved conception. We report a case of endometrial cancer treated by hormone therapy who subsequently presented with a small-foci of recurrence after three conceptions.

Methods: A 33 year-old patient with grade 1, stage IA endometrioid adenocarcinoma of endometrium, received fertility-sparing treatment with high dose megestrol acetate.

Results: Complete response was achieved after 6-months of treatment by dilatation and curettage (D&C). Follow-up endometrial curettages were obtained at intervals of 12 weeks. After 2 unsuccessful pregnancy (one missed abortion, one blighted ovum) a successful conception occurred after a two year of follow up by IVF program. She delivered at term and underwent comprehensive hysterectomy at 14 months of delivery with normal follow-up endometrial curettages. Final pathology revealed a foci of endometrial residual tumor with surgical stage of IA, G1.

Conclusion: The fertility-sparing treatment is feasible in endometrial cancer patient. Recurrence was noted even after pathological remissions, therefore definitive hysterectomy is suggested after the completion of the family.
Poster Session III

TREATMENT OF LOW GRADE ENDOMETRIAL STROMAL SARCOMA

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Objectives: The aim of this study was to obtain information on the prognosis and treatment of the low grade endometrial stromal sarcoma.

Patients and methods: Three patients with low grade endometrial stromal sarcoma treated in kangnam St. Mary’s hospital between 2001 and 2010 were evaluated. The clinical stage, management and outcome were analyzed.

Results: Those patients with low grade endometrial stromal sarcoma had a long overall survival in the presence of receiving hormonal therapy after initial surgery. Eight patients were alive and disease-free status, five had shown a partial response to hormonal treatment, and three were alive with disease on no therapy.

Conclusion: Surgery is the primary treatment for low grade endometrial stromal sarcoma. High dose hormonal replacement as adjuvant therapy will be associated with a lengthened overal survival in patients with low grade endometrial stromal sarcoma.
THE EXPRESSION AND SIGNIFICANCE OF BIGLYCAN IN ENDOMETRIAL CANCER

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Objective: To investigate the expression of Biglycan in endometrial cancer and its clinical significance.

Methods: Detection of Biglycan expression in normal endometrium, atypical endometrial hyperplasia and endometrial cancer using immunohistochemical staining; detection of biglycan expression in serum and ascites from normal cases, atypical hyperplasia and endometrial cancer using ELISA.

Results: (1) Biglycan expression in poorly differentiated group was higher than in well differentiated groups (P < 0.05); (2) the prognosis of patients with positive expression of Biglycan was poorer than the patients with negative expression (P < 0.05); (3) biglycan expression in endometrial cancer tissue and adjacent tissues showed a significant correlation (r = 0.343, P = 0.012); (4) the content of biglycan in the serum and ascitic fluid of patient with endometrial cancer was significantly higher than that in normal control and atypical hyperplasia (P < 0.05); (5) Biglycan expression in serum of patients with endometrial cancer stage III-IV (FIGO) was higher than those with stages I-II (P < 0.05); serum biglycan expression in endometrial cancer with lymph node metastasis was higher than those without metastasis (P < 0.05).

Conclusion: (1) Biglycan plays an important role in the origin and development of endometrial cancer through its action on cancer stroma; (2) Biglycan expression in the stroma of cancer and the prognosis of patients are co-related which could be used as an indicator of the prognosis; (3) detection of biglycan content in serum and ascitic specimen can be used as a basis of differential diagnosis in malignant endometrial tumors.
Poster Session III

CLINICAL AND PATHOGENETIC FACTORS FOR FORECASTING ENDOMETRIAL CANCER

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Objective: Composite estimation of clinical and pathogenetic factors for endometrial cancer (EC) with the regard for organism features and tumors biological activity.

The research of 863 patients with EC was conducted in Almaty Oncology Centre in 1999-2008.

Research methods: Include clinical, ultrasound, hysteroscopic, histologic, immunohistochemical, hormonal, molecular-genetic and statistic studies.

Results: Patients with aggravated heredity of cancer, EC characterized by a more aggressive, resulting in a significantly higher frequency of myometrium invasion in 3.5 times higher than controls ($p<0.05$), the cervix involving 2.9 times higher than in the controls ($p<0.05$), regional lymph metastasis in 3.2% higher than in controls ($p<0.05$), low-grade tumor differentiation in 5.2 times higher than in controls ($p<0.05$) and reduced rates of 3 and 5-year SR of 15.1% and 22.4% respectively, $p<0.05$.

Studying the gene polymorphisms role with EC revealed: the group of patients with EC have higher frequency the gene GSTM1 deletions (49.0% in the control group 36.9%).

Carriage of polymorphic variants of genes SYP1A1 and GSTP1 in patients with EC has no reliable values ($p>0.05$). The I157 gene mutation were found in 4.6% of patient with endometrial cancer. Comprehensive assessment of prognostic factors in EC found that in the pathogenesis of aggressive trends EC and reducing the 5-year SR play a role: aggravated heredity of cancer ($p<0.001$), carrier of the receptor phenotype ER/PR- ($\chi^2=37.721;df=2;p<0.001$), a high level of expression of Her2neu ($\chi^2=3.457;df=1;p<0.07$) and Ki 67>42% ($\chi^2=8.009;df=2;p<0.05$), the presence of the gene GSTM1 ($\chi^2=3.97;p<0.05$).
Poster Session III

A CASE REPORT OF SEGMENTAL ARTERIAL MEDIOLYSIS DEVELOPING IN THE INTERNAL ILIAC ARTERY AFTER OPERATION FOR ENDOMETRIAL CANCER

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Introduction: Segmental arterial mediolysis (SAM) is an arterial disease most commonly reported to involve the splanchnic artery, that often results in life-threatening rupture of the arterial wall, but has rarely been reported in the arteries of the pelvic region. We report a case of SAM in the internal iliac artery, manifesting as a retroperitoneal hematoma, after operation for endometrial cancer.

Case report: A 57-year-old woman underwent modified radical hysterectomy for endometrial cancer, stage Ib G1. About 11 hours after the operation, she went into cardiopulmonary arrest and we diagnosed her as having hemorrhagic shock which followed left retroperitoneal hematoma. A hemostatic operation revealed that left retroperitoneal cavity was filled with a hematoma, and active bleeding was seen from the left iliac artery. Unfortunately, 4 days after reoperation, the patient died of multiple organ failures. An autopsy was performed, which revealed

1) mediolysis in the wall of the internal iliac artery,
2) dissection between the media and adventitia and refilling by thrombus, and
3) evidence of repair in the zones of mediolysis.

These findings were pathologically typical SAM.

Conclusion: Although the pathogenesis of SAM is still uncertain, vasospasm is considered as one of the important factors triggering degeneration of the media of the arterial wall. We would like to call the attention of gynecological surgeons handling around vessels during operations, keeping in mind development of SAM in any pelvic artery.
Poster Session III

RISING TRENDS OF ENDOMETRIAL CARCINOMA IN YOUNGER AND NORMAL WEIGHT WOMEN IN A TEACHING HOSPITAL OF AN ASEAN COUNTRY

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Introduction: Endometrial cancer is the fourth most common cancer worldwide with increasing trend in the Western countries. The association between postmenopausal status and obesity towards endometrial cancer are well known. However, our observation revealed that increasing trend noted in younger and non-obese women.

Objective:

1. To study the incidence and social demographic data of the patients, diagnosed to have Carcinoma Endometrium in University Malaya Medical Centre of Malaysia from 1st January 2005 to 31st December 2009.
2. To study the association between the selected risk factors and occurrence of endometrial carcinoma.

Methodology: Retrospective cohort study of patients with endometrial cancer.

Result: A total of 104 patients were included in this study. Their mean age was 53.71 years. Twelve (11.6%) of these 104 patients were less than 40 years old. Almost half (43.3%) were premenopausal and of endometroid type. Twenty four (23.1%) were patients with BMI of less than 23, and the percentages of lean women and women with younger age group developing cancer of endometrium showed an increasing trend each year over the study period.

Conclusion: Based on our observation, sampling of endometrium should be considered early even in lean and younger women who presented with menorrhagia and not responding to the standard medical treatment.
Poster Session III

IMPORTANCE OF SCREENING REGARDING LYNCH SYNDROME IN ENDOMETRIAL CANCER PATIENTS WITHOUT FAMILY HISTORY

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Objective: Two most common cancers regarding Lynch syndrome are colon and endometrium. There are no concrete guideline for recommending which diagnostic exams (immunohistochemistry (IHC), microsatellite instability (MSI) and gene sequencing) and who should get tests. Other obstacles like inaccurate family history, extensive costs prevent from economical screening. We report one case of Lynch syndrome in endometrial patient without family history of any cancer type.

Case: 55 years old woman visited local clinic for vaginal bleeding. Endometrial biopsy revealed endometrioid type, grade 2. She was referred to Samsung Changwon Hospital for treatment. She undertook MRI and other diagnostic tests. Her CA 125 was 9.06 and no other abnormal mass were visible in imaging tests. Hysterectomy and bilateral salpingooophorectomy was done. After checking negative frozen biopsy of pelvic lymph node, operation has finished. Screening IHC (MLH1, MSH2) was done for this patient. Although she had no family history, screening IHC were done with patient’s agreement. MLH1 was positive 90 percent and MSH2 was negative. According to diagnostic algorithm, MSI and gene sequencing after proper counseling about importance of genetic tests. MSI were done about five markers (BAT25, BAT26, D2S123, D5S346, D17S250). There were two unstable markers (BAT25, BAT26) and it meant MSI-H. Gene sequencing revealed one missense mutation in c.23c>T(p.Thr8Met). Pathology reported here stage was IA and she didn’t get adjuvant treatment. But in-detail counseling of disease and proper exams to check it was done.

Conclusion: This case can give practical information to help gynecologists screen effectively Lynch syndrome patient. Proper genetic screening and counseling should be done for suspicious patients to prevent second cancer in Lynch syndrome.
Poster Session III

ESTABLISHMENT OF CANCER-TISSUE ORIGINATED SPHEROIDS (CTOSS) AND CHEMOSENSITIVITY TEST FOR ENDOMETRIAL CANCER

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Object: In this study, we established a chemo-sensitivity test for endometrial cancer using cancer-tissue originated spheroids (CTOSs). This chemo-sensitivity test can find not only the best regimen for endometrial cancer but also personalized medicine in the future.

Materials and methods: Cancerous tissues were removed from a series of 33 patients with endometrial cancer. By mechanical and chemical treatments, clusters of epithelial cells formed cancer-tissue originated spheroid (CTOS) in stem cell culture medium within 24 hours and can be cultured and expanded, as described by Kondo et. al (PNAS, 2011).

Results: Spheroid formation was observed in all of 33 cases, including 29 cases of endometriod adenocarcinoma (G1:21 G2:3 G3:5), 2 cases of serous adenocarcinoma, and 2 cases of mixed carcinoma (serous and endometrioid adenocarcinoma), within 24 hours. Some of these spheroids were able to be transplanted to subcutaneous of immune-deficient mice and formed tumors. These xenograft tumors showed quite similar histopathology for their original tumors. For chemo-sensitivity test, spheroids were exposed to cisplatin for 10 hours at day7, and evaluated at day14. The spheroids growth was inhibited in a dose-dependent manner.

Conclusion: For endometrial cancer, establishment of CTOSs allow us to analyze chemo-sensitivity and gives a prediction of the efficacy of anti-cancer agents for personalized medicine.
Poster Session III

POSTOPERATIVE VAGINAL BRACHYTHERAPY ALONE IN ENDOMETRIAL CANCER


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Introduction: The aim was to determine the clinical characteristics and outcomes in early staged endometrial cancer patients treated with vaginal cuff brachytherapy alone.

Methods: Between 1999 and 2011, a total of 75 patients who received postoperative vaginal cuff brachytherapy alone were evaluated retrospectively. All clinical and pathological variables were analyzed by univariate and multivariate analysis.

Results: The mean age was 58 years (range, 37-80). Median follow-up was 38 months (range, 5-151 months). All patients received brachytherapy following surgery. Stage was assigned according to the FIGO 2010 definition. Stage distribution was as follows: 34 patients (45%) stage IA, 35 patients (47%) stage IB, and 6 patients (8%) stage II. Grade distribution was as follows: 32 patients (43%) Grade 1, 36 patients (48%) grade 2, and 7 patients (9%) grade 3. Overall survival was 91% at 2 years. By the end of follow up, 67 patients (89%) were disease-free, 2 (2%) were alive with disease and 6 (8%) were died with other reasons. No patient treated with vaginal cuff brachytherapy alone developed Radiation Therapy Oncology Group grade 3-4 toxicity. Univariate and multivariate analyses identified only stage as significant predictors for overall survival.

Conclusions: Postoperative vaginal cuff brachytherapy alone provides high local control rates and survival with acceptable toxicity in patients with early staged endometrial carcinoma.
**Poster Session III**

**SERUM VEGF, VEGFR1 AND VEGFR2 IN PATIENTS WITH UTERINE SARCOMA**

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**Background:** In many tumors is observed over expression of VEGF, VEGF receptor-1 and 2. It seems that serum levels of VEGF and their receptors may be elevated in uterine sarcoma patients. The purpose of this study was to evaluate the potential use of serum levels of VEGF, VEGFR1 and VEGFR2, as compared with CA125, to improve the diagnosis of uterine carcinosarcoma.

**Methods:** The sera of 54 untreated patients were examined. Sera of 40 healthy women were served as controls. Concentrations of VEGFR1 (sFLT1) were determined using the Roche instruments system, VEGF and VEGFR2 by the ELISA of R&D, CA125 by the Abbott kits. For the statistical analysis, Mann-Whitney U tests were applied. Receiver-operating characteristic (ROC) curves were used, to assess the diagnostic sensitivity and specificity of the marker results.

**Results:** In uterine sarcoma patients, as compared with controls, there were significantly higher serum levels of VEGF (p< 0.00001) and VEGFR1 (p< 0.0001). In the study group, elevated VEGF concentration was the most frequently observed in 62% of cancer patients; while the concentration of CA125 was elevated in 28%, VEGFR1 in 25%, VEGFR2 in 17% of patients. The concentration of VEGF revealed higher sensitivity than CA125, with areas under ROC curve of 0.946 and 0.791 respectively, but VEGFR1, VEGFR2 0.730 and 0.605.

**Conclusions:** Assessment of VEGF complementary to the tumor marker CA125 testing might improve the diagnostic sensitivity of laboratory tests performed in patients with uterine sarcoma. Further studies will evaluate the clinical utility of the serum antiangiogenic factors VEGFR1 and VEGFR2 levels.
Poster Session III

METHYLATION ANALYSIS OF TUMOR SUPPRESSOR GENES IN ENDOMETRIAL CANCER

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Objective: Epigenetic changes are considered to be a frequent event during tumor development. Hypermethylation of promoter CpG islands represents an alternative mechanism for inactivation of tumor suppressor genes, DNA repair genes, cell cycle regulators and transcription factors. The aim of this study was to investigate promoter methylation of specific genes in endometrial cancer by comparison with normal endometrial tissue.

Methods: To search for epigenetic events we used MS-MLPA (Methylation-specific Multiplex ligation-dependent probe amplification) to compare the methylation status of 20 tissue samples of endometrial cancer with 9 control samples.

Results: Using a 15% cut-off for methylation, we observed significantly higher methylation in CDH13 gene in the endometrial cancer group. We also observed higher methylation in WT1 and CD44 genes in endometrial cancer, but with no statistical significance cause of the small amount of analyzed samples.

Conclusion: These findings could potentially be used in screening of endometrial cancer, and may have implications for future therapeutic strategies based on epigenetic changes.

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Poster Session III

RETROSPECTIVE ANALYSIS OF PATIENTS WITH UTERINE CARCINOSARCOMA

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Background: The purpose of this study was to determine the clinical characteristics, patterns of recurrence and survival outcomes in patients with uterine carcinosarcoma treated in our institution.

Methods: Records of the patients with uterine carcinosarcoma were retrospectively evaluated and 26 pts with carcinosarcoma diagnosed between 2007 and 2011 were identified. All patients were initially treated surgically by the same surgeon with comprehensive staging, i.e. total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and paraaortic lymph node dissection and omentectomy. Demographic features, tumor characteristics, treatment regimens and patient outcomes in terms of DFS and OS were analyzed.

Results: Median age was 61 (range 43-78). 10 patients (38%) had stage I disease, 3 patients (12%) had stage II, 4 patients (15%) had stage III and 9 patients (35%) had stage IV disease at diagnosis. Sixteen patients (62%) received chemotherapy with paclitaxel and carboplatin for 6 cycles. Two patients received radiotherapy. Median follow up was 17 mos. Sixteen patients relapsed and 13 died on follow up. One out of 16 relapses was lung metastases and all the remaining were intraabdominal. 3 year DFS was 37%. 3 year OS was 30%.

Conclusions: Our data show that uterine carcinosarcomas tend to be more at more advanced stage at diagnosis and despite the use of chemotherapy and radiotherapy, overall prognosis is poor. Surgery remains the mainstay of treatment. More effective adjuvant strategies are needed to reduce relapse and death rates.
Poster Session III

IMPACT OF METFORMIN USE IN DIABETIC WOMEN RECEIVING ENDOMETRIAL CANCER TREATMENT

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We investigated whether metformin use in diabetic women receiving endometrial cancer treatment lowered cancer relapse and cancer-related death. We reviewed metformin use in 312 non-diabetic and 92 diabetic women (total n=404) who underwent surgery, chemotherapy, or radiation for corpus-confined stage I or II endometrial cancer between 1995 and 2010. Endometrial cancer relapse rates, disease-free survival (DFS), and overall survival (OS) were calculated. Demographic, body mass index, and tumor variables were balanced. Median follow-up was 66 months. 40 (43%) of 92 diabetic women used metformin for a median 5.5 weeks prior to surgery. Endometrial cancer relapses occurred in 47 (15%) of 312 non-diabetic and 21 (23%) of 92 diabetic women (p=0.08). Relapse rates were similar among diabetics who used metformin (9 [23%] of 40) and those diabetics who did not (12 [23%] of 52, p=0.95). After pelvic radiation (1.8 Gy x 25 daily fractions) or intravaginal brachytherapy (7 Gy x 3 once weekly fractions), diabetic users of metformin had similar rates of relapse (4 [19%] of 21) as any woman who did not (31 [14%] of 224, p=0.52). 5-year estimates of cancer-related death was similar among diabetics (10%) and non-diabetics (6%, p=0.58). Median OS was longer in non-diabetics (185 months), as compared to diabetics (116 months, p=0.004). Preliminary data in diabetic women receiving endometrial cancer treatment show limited impact of metformin use. We plan further study to understand any benefit of metformin use in cancer treatment, especially during radiotherapy.
Poster Session III

HETEROGENEITY OF EX VIVO CHEMOSENSITIVITY OF ENDOMETRIAL CARCINOMAS: IMPACT OF THE HISTOLOGICAL SUBTYPE

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Objective: This study was set up to analyze the heterogeneity of ex vivo chemosensitivity of endometrial carcinomas (ECs) with a special focus on the histological subtype.

Methods: We used chemosensitivity profiles of 46 native EC specimens successfully tested with the ATP-based tumor chemosensitivity assay (ATP-TCA): type I EC (EC-I, i.e. endometrioid, squamous, adenosquamous), n=25; type II EC (EC-II, i.e. papillary-serous, clear cell, carcinosarcoma), n=21. The following single agents and combinations were tested at least ten times in both EC-I and EC-II and were thus considered for this analysis: doxorubicin (DOX, n=14/18), mitoxantrone (MXN, n=13/14), cisplatinum (DDP, n=18/20), paclitaxel (PCT, n=17/20), gemcitabine (dFdC, n=11/10), DOX+PCT (AT, n=19), MXN+PCT (NT, 13/18), PCT+DDP (TP, n=14/18), 4-OH-cyclophosphamide+DDP (CP, n=12), DDP+dFdC (PG, n=11). Each regimen was tested at a 1.5 log dose range covering six therapeutical and supratherapeutical concentrations. Ex vivo response rates (EVRRs) were calculated after classifying a tumor as resistant or sensitive using a semiquantitative score.

Results: In EC-II vs EC-I, the EVRR was significantly higher towards DOX (22% vs 14%), AT (89% vs 67%), and PG (91% vs 58%) and significantly lower towards DDP (5% vs 33%), PCT (40% vs 53%), and TP (67% vs 79%). The EVRR for MXN (29% vs 31%), dFdC (30% vs 27%), CP (83% vs 83%), and NT (89% vs 85%) was comparable in both groups.

Conclusions: EC-II is a distinct tumor entity with major phenotypical differences to EC-I but also to ovarian carcinomas due to their marked intrinsic resistance against DDP and PCT.
Poster Session III

RAD21 AND RUNX1 EXPRESSION IN ENDOMETRIAL CANCER

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Introduction: Endometrial cancer is the most frequent malignancy of the female genital tract. but the understanding of its molecular background still remains insufficient.

Aim of the study: In the view of poor understanding of the molecular background of endometrial cancer we have attempted to identify new markers which may: correlate with patients’ clinicopathological features; further elucidate molecular pathways of endometrial carcinogenesis; help in type I and type II differentiation.

One of the key elements worth investigating in this particular context are cohesins and their role in cancer formation. It has been discovered that deregulation of cohesin expression and cohesin-regulated genes is common in numerous human cancers. In the present work we attempted to determine the role of RAD21 and RUNX1 in endometrial cancer. The first protein is a component of the cohesin complex, crucial for chromosome segregation and DNA repair. The latter is the transcription factor implicated in RAD21 regulation.

Materials and methods: 144 endometrial cancer tumors have been studied in the context of RAD21 and RUNX1 expression profiles. RNA levels were measured with the use of reverse transcription quantitative PCR. RAD21 gene dosage was determined by quantitative PCR.

Results: RAD21 gene dosage was significantly associated with RAD21 mRNA expression (ρ=0.22; p=0.009). Furthermore, RAD21 expression strongly correlated with RUNX1 expression (ρ=0.43; p<0.0000001). RAD21 and RUNX1 status correlated with some clinicopathological features of the endometrial cancer patients.

Conclusions: Our results clearly demonstrate that the mRNA expression of RAD21 and RUNX1 is deregulated and co-dependent in endometrial cancer cells.
HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN WOMEN FOLLOWING ROBOTIC SURGERY FOR ENDOMETRIAL CANCER

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Objective(s): Prospective evaluation of surgical and health-related quality of life (HRQoL) outcomes of women with endometrial cancer undergoing robotic-assisted surgery to determine the relationship between BMI and age, and the physical, functional, and psychosocial areas of HRQoL, and patient satisfaction.

Study methods: During the first two years of the robotics program, data concerning patient demographics and surgical outcomes was collected prospectively. At the first post-operative visit, all participants completed an HRQoL questionnaire. The association between BMI and age, as well as the different HRQoL areas was examined using Chi-square and ANOVA.

Results: Overall 109 patients were investigated, 41 patients were 70 years or older and 51 had a BMI of 30 or greater. Following surgery, the mean hospital stay was 1.9 (±1.5) days and reported pain level was highest on day 2 with a score of 3.4 (±2.1) on a scale of 7. Moreover, two thirds of women reported no pain by the post-operative visit and only 18.2% of women in the 70 years or older cohort used any narcotic for pain control. Results indicated there was little influence of the surgery on HRQoL and women resumed typical activities within an average of 11 days. Lastly, participant average rate of satisfaction was 6.7 on a scale of 7.

Conclusion(s): Patients benefited from robotic surgery regardless of age or BMI. This pilot study demonstrates the HRQoL advantages of robotic-assisted surgery for endometrial cancer.
GENETIC POLYMORPHISM OF PRKCDBP IS ASSOCIATED WITH AN INCREASED RISK OF ENDOMETRIAL CANCER

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Objective: PRKCDBP is a putative tumor suppressor located at 11p15.4, at which frequent genomic loss has been observed in several human cancers. We explored the possible association of an intraexonic single nucleotide polymorphism (SNP) of rs1051992, which results in a Leu to Pro substitution, with increased risk for endometrial carcinogenesis.

Methods: Endometrial cancer tissues from 147 cancer patients and 191 healthy individuals were included for the test for rs1051992 genotypes by restriction endonuclease PvuII-based genotyping. Allele frequencies in cancer specimens were compared with those in healthy controls. We also evaluated the association between polymorphism and histopathological features.

Results: Individuals with variant homozygous CC genotype had increased risk of endometrial cancer as compared to those with carrying T genotype (OR=1.62, 95% CI 1.051-2.501, p=0.019). And the CC genotype was significantly associated with the early stage and grade 1 tumor.

Discussion: Although the number of specimens used in this study is not enough, this study raises the possibility that the PRKCDBP rs1051992 SNP might be associated with endometrial cancer development.
Poster Session III

PREOPERATIVE RADIOTHERAPY FOR CLINICAL STAGE II ENDOMETRIAL CANCER: IS IT TIME TO REVISE THE TREATMENT PARADIGM?

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Objective: To review recurrence patterns and survival outcomes of women receiving preoperative radiotherapy for clinical stage II endometrial cancer in British Columbia.

Methods: Retrospective population-based cohort study of all clinical Stage II endometrial cancer patients referred to the British Columbia Cancer Agency from 2000 to 2008, deemed ineligible for primary surgery and therefore offered preoperative radiotherapy followed by surgery. Patient demographics, uterine risk factors, timing and details of treatments, and timing and sites of recurrence were obtained from patient records. Primary outcome measures were sites of recurrence and recurrence-free survival.

Results: There were 29 patients with a mean age of 61 (range 41-83 years) and median follow-up of 3.1 years (0.3-5.3 years). Three year overall survival was 79%, and median recurrence-free survival was 2.5 years. Eight patients recurred (27.6%), with a median time to recurrence of 1.3 years, (range 0.4-2.7). Six of these 8 women had 2 or more high-risk uterine factors (deep myometrial invasion, grade 3 tumor), ovarian involvement, or adverse histological type (carcinosarcoma), compared to only 1 of 21 patients who did not recur. Seven out of 8 women recurred outside the radiated volume. Median survival after recurrence was 1.0 years (0.4 - 2.2 years).

Conclusions: Women with clinical stage II endometrial cancer have a significant risk of recurrence when treated with preoperative radiotherapy followed by surgery. Women who recurred more often had distant recurrences and were more likely to have high-risk factors on uterine pathology.
**Poster Session III**

**MOLECULAR PROFILES OF MICRORNA IN ENDOMETRIAL CARCINOMA USING FORMALIN-FIXED PARAFFIN-EMBEDDED (FFPE) TISSUE SAMPLES**

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**Objectives:** This study was performed to provide the candidate miRNAs for further confirming the role of miRNAs in carcinogenesis of endometrioid adenocarcinoma using formalin-fixed paraffin-embedded (FFPE) tissue samples.

**Materials and methods:** We investigated the differences in miRNA expression profile in 8 fresh frozen tissues (4 endometrioid adenocarcinoma, 4 normal endometrium) using human miRNA microarray. Then we tested whether the same results can be obtained with RNAs purified from FFPE samples in miRNA expression studies. We next tested whether specific inhibition of overexpressed microRNAs would alter the chemosensitivity.

**Results:** The miR-200a*, miR-200b*, miR-141, miR-182, and miR-205 were greatly enriched in cancer tissue in microarray results. The expressions of these 5 miRNAs were validated using quantitative real time reverse transcription-PCR (qRT-PCR). Then, I performed qRT-PCR profiling of miR expression in 30 formalin-fixed paraffin-embedded (FFPE) specimens (20 endometrioid adenocarcinoma, 10 non-tumor specimens) and reconfirmed the results of differential expression between cancer and normal tissue. In in vitro cell viability assay, anti-miR200b* slightly enhanced cisplatin cytotoxicity compared with negative control although it showed marginal statistical significance (p=0.07).

**Conclusion:** This information provided the candidate miRNAs for further confirming the role of miRNAs in carcinogenesis of endometrioid adenocarcinoma, and also provided that FFPE specimens can be successfully used for real-time PCR based quantitative miRNA expression studies.
Poster Session III

ACCURACY OF MRI AND INTRA-OPERATIVE FROZEN SECTION FOR EVALUATING RISK FACTORS ASSOCIATED WITH LYMPH NODE METASTASIS IN ENDOMETRIAL CANCER


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Objective: To evaluate the accuracy of magnetic resonance imaging (MRI) and intra-operative frozen sectioning (IFS) for evaluating risk factors associated with lymph node (LN) metastasis in surgically staged endometrial cancer patients.

Methods: The medical records of 175 endometrial cancer patients, who underwent comprehensive surgical staging including pelvic and para-aortic LN dissection between January, 2008 and July, 2011 were retrospectively analyzed. Results of MRI and IFS of the uterus for the evaluation of risk factors were correlated with final pathology.

Results: Our results showed a high specificity and negative predictive value (NPV) of MRI and IFS for evaluation of myometrial invasion (MI) and cervical stromal invasion. Of the 41 patients identified as low-risk by both MRI and IFS, none had pelvic or para-aortic LN metastases in the final pathology.

Conclusions: The results indicate that MRI and IFS are useful for the evaluation of risk factors associated with LN metastasis in endometrial cancer patients. MRI and IFS can be used to accurately identify low risk patients who do not need comprehensive surgical staging and to prevent the associated morbidities.
Poster Session III

THE IMPACT OF LYMPHOVASCULAR SPACE INVASION ON RECURRENCE AND SURVIVAL IN PATIENTS WITH EARLY STAGE ENDOMETRIAL CANCER


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Objectives: To evaluate the relationship between lymphovascular space involvement (LVSI) in early stage of endometrial cancer on recurrence and survival.

Materials and methods: From 1991 through 2010, 560 patients with a diagnosis of endometrial carcinoma were treated at University Hospital of Bari, Italy. The Log-Rank test and Kaplan-Meyer methods were used for time-to-event analysis to evaluate the effects of LVSI on recurrence rate and survival time.

Results: Of the 560, 525 underwent primary surgery. Of those who underwent surgery, 399 had early stage. Three hundred and forty women were not found to have LVSI, whereas 59 were found to have LVSI. Forty-nine (12%) patients developed a recurrence. Of the them, 20 were found to have LVSI. The statistical analysis showed that LVSI was strongly associated to the occurrence of relapses (p < 0.0001) and poor survival (p < 0.0001).

Conclusions: The presence of LVSI should be included in the clinical decision to decide whether or not a patient with early stage endometrial cancer is at high risk of recurrence and should receive adjuvant therapy, because the presence of LVSI is associated with a high risk of recurrence and poor overall survival.
Poster Session III

THE IMPACT OF MULTIMODALITY THERAPY ON SURVIVAL FOR NEWLY DIAGNOSED UTERINE CARCINOSARICOMA

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Objectives: To investigate treatment outcomes of patients with uterine carcinosarcoma (CS) who received the complete surgical resection of all visible disease and platinum-based adjuvant chemotherapy.

Methods: We conducted a retrospective review of 127 patients with uterine CS treated at our institution 1990 to 2010. We operated 123 patients of clinical stage 1-3 uterine CS. 97 of them underwent complete resection and systemic lymphadenectomy. Their clinical, surgical and pathological data were reviewed. We defined the multimodality therapy as complete surgical resection of all visible disease and platinum-based adjuvant chemotherapy.

Results: 97 eligible patients (Pathological stage in FIGO2008 was Stage1:50, stage2:6, stage3:37, stage4:4) underwent surgical staging including pelvic lymphadenectomy, and 76.3%(73/97) patients received Para-aortic lymphadenectomy. They received median 5 cycles of platinum-based adjuvant chemotherapy. multimodality therapy was associated with median Overall survival (OS) of 50.3months versus 26.6months in patients with incomplete multimodality therapy (P< 0.05). After multimodality therapy, 32.9%(32/97) patients had recurrence, and 24/32 with hematogenous recurrence, 5/32 Lymphogeneous recurrence. Lymph node metastasis and Myometrial invasion was clearly related to OS,OR2.53(1.88-5.34),OR1.41(1.41-11.8).

Conclusion: The combination of complete surgical resection of all visible disease and platinum-based adjuvant chemotherapy may effective treatment. but, the hematogeneous metastasis had not a significantly lower level, despite the full treatment. The role of multimodality treatment in uterine CS warrants further investigation.
Poster Session III

TREATMENT OF PURE UTERINE SARCOMA AT THE INSTITUT CATALÀ D’ONCOLOGIA

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Aims: Uterine sarcomas are especially rare tumours (3% - 5% of uterine cancers), characterized by histopathological diversity, rapid clinical progression and poor prognosis. In the last decade, the pathological description of uterine sarcomas has experience numerous changes. Carcinosarcoma (CS) had traditionally been considered a sarcoma. CS has therefore now been re-classified as a dedifferentiated/metaplastic endometrial carcinoma, and for this reason it is not included in our study. The aim of this retrospective study was to investigate the clinical and histopathological characteristics of the disease and treatment outcome of patients with pure uterine sarcomas.

Materials and methods: All patients with pure uterine sarcoma histology treated at the Institut Català d’Oncologia in Barcelona, between 2002 and 2010 were reviewed.

Results: 17 patients treated over an 8-year period were obtained. Nine patients (53%) had leiomyosarcoma, 7 (41%) had endometrial stromal sarcoma, and 1 patient had unclassified sarcoma. All were treated with external beam radiation after surgical excision. Mean age was 62 years (51- 69 y). 13 patients (76%) presented with stage I, 2 (12%) stage II, and 2 (12%) stage III. The overall actuarial 2-year survival estimate was 82.5%. Two patients experienced local relapse. The 2-year local control rate was 90%. Five patients experienced either local or metastatic relapse. The 2-year progression free survival rate was 58%.

Conclusions: In our experience, combined treatment (surgery and adjuvant radiation therapy) is effective. No other treatment modality seems to be as effective as the combined treatment of hysterectomy with bilateral oophorectomy and adjuvant radiation therapy.
Poster Session III

CAN WE SAFELY OMIT PARA-AORTIC LYMPHADENECTOMY FROM THE SURGICAL STAGING OF WOMEN WITH INTERMEDIATE AND HIGH-RISK ENDOMETRIAL ADENOCARCINOMA?

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Objectives: To characterize clinical outcomes in patients with intermediate or high-risk endometrial carcinoma who underwent surgical staging with or without para-aortic lymphadenectomy.

Methods: This is a retrospective cohort study of patients with intermediate or high-risk endometrial adenocarcinoma who underwent surgical staging with (PPALN group) or without (PLN) para-aortic lymphadenectomy. Data were collected, Kaplan-Meier curves generated and univariate and multivariate analyses performed to compare differences in adjuvant therapy, disease recurrence, disease free survival (DFS) and overall survival (OS).

Results: 118 patients were included in the PPALN group and 139 in the PLN group. Patients in the PPALN group were more likely to receive adjuvant vaginal brachytherapy (25.4% vs 11.5%, OR=2.5, p=0.03) and less likely to receive adjuvant multi-modal combination therapy (17.8% vs 28.8%, OR=0.28, p=0.002). DFS was improved in the PLN group as compared to PPALN (80% vs 62%, p=0.02). OS was equivalent (p=0.93). Patients in the PPALN group who had less than 10 para-aortic nodes removed were twice as likely to recur than patients who had 10 or more para-aortic nodes or patients in the PLN group (HR 2.08, CI 1.20-3.60, p=0.009).

Conclusions: Patients in the PLN group were more likely to receive multi-modal adjuvant therapy and had better DFS than the PPALN group. Pelvic lymphadenectomy followed by adjuvant radiation and chemotherapy may represent an effective treatment option for patients with intermediate or high-risk disease. If systematic para-aortic lymphadenectomy is performed and less than 10 para-aortic lymph nodes are obtained, multi-modality adjuvant therapy should be strongly considered to improve DFS.
Poster Session III

PIPELLE BIOPSY VERSUS CURETTAGE IN ACCURACY OF PRE-OPERATIVE GRADING OF ENDOMETRIAL CANCER


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Background and aims: Pre-operative endometrial cancer grade is used to plan extent of surgery offered to women in the UK. This study aimed to compare clinic Pipelle biopsy and operating room curette for diagnostic accuracy of detection of poorly differentiated disease.

Methods: A prospective diagnostic accuracy study was performed to assess the correlation between pre-operative tumour grade as diagnosed by curette and Pipelle biopsy and findings in consecutive hysterectomy specimens in 158 women. All specimens were reviewed in a central tumour board/MDM.

Results: Sensitivity of Pipelle for diagnosis of poorly differentiated disease was 0.89 (95% CI 0.64 to 0.98), corresponding value for curette was 0.94 (95% CI 0.82 to 0.99). Specificity of Pipelle was 0.98 (95% CI 0.84 to 0.99) and curette specificity was 0.93 (95% CI 0.85 to 0.97). Positive predictive value was 0.96 (95% CI 0.72 to 0.99) for Pipelle was 0.85 (95% CI 0.71 to 0.93) for curette. Negative predictive value was 0.94 (95% CI 0.79 to 0.99) for Pipelle and 0.98 (95% CI 0.91 to 0.99) for curette.

Conclusions: Pipelle biopsy is equally accurate as curette in diagnosis of poor differentiation of endometrial cancer. Both methods are sensitive and specific and have high negative predictive values. This provides further reassurance that using biopsy result to plan extent of surgical treatment is a safe strategy.
Poster Session III

MOLECULAR PROFILING OF ENDOMETRIAL CARCINOMA SUBTYPES; THE RATIONALE FOR MOLECULAR CLASSIFICATION

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The histopathological classification of endometrial carcinomas (EC) is based on grade and tumour cell type; endometrioid, serous, carcinosarcomas, mixed and clear cell subtypes are associated with distinct molecular alterations and prognosis. The current classification system for diagnostically challenging high-grade subtypes has been limited in its reproducibility and prognostic abilities. Molecular profiling may allow for subclassification of problematic cases, thus improving reproducible diagnoses of endometrial carcinomas.

392 endometrial carcinoma cases were sequenced using exon capture including the genes; PTEN, PIK3CA, ARID1A, KRAS, CTNNB1, PPP2R1A, TP53, BRAF, PPP2R5C. An additional four genes; PIK3R1, PIK3R2, FGFR, FBXW7 were sequenced in 159 of the 392 tumours.

We found that endometrioid carcinomas are defined by mutations in PTEN, PIK3CA, ARID1A, however high-grade endometrioid carcinomas have an increased frequency of TP53 mutations. Serous carcinomas are a distinct subtype with mutations in TP53 and PPP2R1A. Using mutation profiles we were able to distinguish outliers, where the profile did not fit with the original diagnosed subtype. After careful review, the majority of these outliers were tumours with challenging diagnosis, often with mixed morphology, where the original diagnosis was incorrect. Carcinosarcomas were found to have profiles of either endometrioid-like or serous-like mutations.

Using mutational profiles we have shown distinct features of the differing endometrial subtypes. We identified an intermediate subtype, often with mixed endometrioid and serous carcinomas morphology, where the diagnosis can be refined using mutation profiles. This molecular classification may aid in improving reproducible diagnosis and to identify patients that may benefit from targeted therapeutics.
Poster Session III

EVALUATION OF THE DEPTH OF MYOMETRIAL INVASION BY TRANSVAGINAL ULTRASOUND IN ENDOMETRIAL CANCER PATIENTS. OUR EXPERIENCES IN 168 PATIENTS

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The depth of myometrial infiltration by endometrial cancer is an important prognostic factor. The examination of the depth of infiltration splits the patients into the low- and high-risk groups and thus influences the therapeutic procedure. Transvaginal ultrasonography represents a first-choice diagnostic test for the assessment of the depth of myometrial infiltration as the time consumption and financial demands of magnetic resonance imaging need to be taken into account. We study our EC patients in the period January 2009 - March 2012. Analysed were the results from 168 patients who had been examined with the TVS at the Department of Oncogynecology of St. Elizabeth Cancer Institute in Bratislava. Correlated firstly with the preoperative and then secondly with the definitive histopathological examination was the depth-of-infiltration-related data that had been taken from the sonographic findings. The output being monitored was the exclusion or acknowledgment of the invasion exceeding half the thickness of myometrium. In our study, the diagnostic accuracy of the method reached 83.9%, while the other indicators were as follows: sensitivity 92.3 %, specificity 79.2%, positive predictive value (PPV) 61.0 %, negative predictive value (NPV) 96.7 %, the credibility ratio of positive test 4.455 and the credibility ratio of negative test 0.097 with 95% CI.

The results of the depth of myometrial infiltration examination and their comparison with the data from similarly oriented clinical studies entitle us to include this examination in the set of standard preoperative methods used for the examination of patients with endometrial carcinoma.
Poster Session III

THERAPEUTIC DOSES OF METFORMIN SUPPRESSES CELL PROLIFERATION OF ENDOMETRIAL CANCER IN VIVO

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Background: Metformin, a widely used anti-diabetic drug, is thought to suppress oncogenesis in several malignancies. In vitro studies have demonstrated a direct anti-proliferative effect of metformin; however, this effect was demonstrated only with high doses of metformin. It is unclear if therapeutic doses of metformin are effective for patients with endometrial cancer.

Methods: The effects of metformin were investigated in endometrial tissues obtained from 15 patients with stage I endometrial cancer who received metformin (1500-2250 mg/day) before surgery. The Ki67 labeling index, a marker for cell proliferation, was compared before and after surgery. Activation of the MAPK, AMPK, and mTOR signaling pathways, as well as cell-cycle proteins, was evaluated by western blotting. Plasma and tissue levels of metformin were analyzed using liquid chromatography tandem-mass spectrometry.

Results: Metformin had anti-neoplastic effects in patients with endometrial cancer at therapeutic doses (1500-2250 mg/day) in diabetic patients. Plasma and tissue levels of metformin did not exceed 0.03 mM at doses of 750 mg 3 times daily. Preoperative metformin treatment reduced stain uptake when stained for phospho-ERK, phospho-S6, and reduced the ki-67 labeling index significantly (p = 0.031). Conforming to in vitro data, preoperative metformin therapy increased AMPKa phosphorylation (p = 0.026), decreased S6 phosphorylation (p < 0.01), decreased ERK1/2 phosphorylation (p < 0.01), and alteration of cell cycle protein contradict G1 arrest.

Conclusion: The anti-neoplastic activity of metformin was demonstrated in vivo at therapeutic doses. These results suggest metformin accomplished AMPK-m TOR and ERK1/2 suppression via an indirect action.
PRELIMINARY ANALYSIS OF COMBINATION CHEMOTHERAPY WITH IRINOTECAN AND PLATINUM FOR PATIENTS WITH RECURRENT ENDOMETRIAL CARCINOMAS


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Objective: The aim of this study is to evaluate effects and toxicities of combination therapy with irinotecan hydrochloride (CPT-11) and platinum (CPT-Pt) for recurrent and refractory EMC retrospectively.

Material and methods: Between 2000 and 2012, twelve patients which received CPT-Pt for recurrent EMC at our hospital were identified. CPT-Pt consisted of 40-70mg/m2 of CPT-11 on days 1, 8, and 15, and 50-60 mg/m2 of cisplatin or nedaplatin on day 1, q4weeks.

Results: Median age of the patients was 59 years, and median prior chemotherapeutic regimens ranged from 1 to 3. Two patients had prior pelvic irradiation. RR defined as the ratio of complete remission (CR) and partial remission (PR) of CPT-Pt therapy was 3 of 12 (25%), and clinical benefit rate (CBR) including disease stabilization was 6 of 12 (50%). Six (50%) cases developed hematologic toxicities more than grade 3, 3 cases had grade 3/4 febrile neutropenia and one (8%) case had grade 3 diarrhea. All cases recovered with conservative treatment. Patients with the wild-type UGT1A1 had higher dose of CPT-11 (p=0.01) but similar incidence of grade 3/4 toxicities, RR and CBR compared with patients with UGTA1A*6 and *28.

Conclusion: CPT-Pt regimen showed promising activity for recurrent and refractory EMC, and toxicities were tolerable. Furthermore, CPT-11 would decrease adverse effects and preserved RR modifying the dose of CPT-11 according to UGT1A1 polymorphisms. This regimen would be a candidate for further investigation for EMC.
Poster Session III

A COMPARISON OF PATHOLOGIC FEATURES AND CLINICAL OUTCOMES OF GRADE III ENDOMETRIOD ADENOCARCINOMA AND SEROUS CARCINOMA OF THE UTERUS

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Aim: To compare the pathologic characteristics and treatment outcomes of patients with grade III endometriod carcinoma (EC) and serous carcinoma (SC) of the uterus without myometrial invasion.

Methods: A retrospective multi-institutional study of grade III EC and SC cases from 1989-2011 was completed. Cases without myometrial invasion were extracted. Demographic characteristics, pathologic features, treatment and recurrence data were compared.

Results: Fifteen cases of grade III EC and 55 cases of SC without myometrial invasion were identified. 80% of patients in both groups had stage IA disease. Stage II disease was found in 2 EC cases and 1 SC case. One EC patient and 9 SC patients had advanced stage disease. None of the EC cases displayed evidence of angiolymphatic invasion, compared to 22% (12/55) in the SC group. Lymph node dissection was completed in the majority of cases, 80% (12/15) of EC cases and 60% (33/55) of the SC cases. Eight (53%) grade III EC patients and 27 (49%) SC patients received no adjuvant therapy. Radiation therapy was the most common form of adjuvant therapy in the EC group (N=5) while chemotherapy was more common in the SC group (N=21). Recurrences were reported in 27% (N=4) of patients with grade III EC and 15% (N=8) with SC.

Conclusion: In a small retrospective multi-institutional study, patients with grade III EC without myometrial invasion had a significant risk of recurrence in the absence of angiolymphatic invasion. Radiation therapy was the most common form of adjuvant treatment in that population.
Poster Session III

IS PLATINUM FREE INTERVAL FOLLOWING PRIMARY CHEMOTHERAPY A PREDICTIVE FACTOR OF SURVIVAL AFTER SECOND-LINE CHEMOTHERAPY IN RECURRENT ENDOMETRIAL CANCER?

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**Background:** The applicability of the concept of “platinum sensitivity” had not been assured in recurrent endometrial cancer. The aim of this study is to evaluate whether platinum free interval (PFI) following primary platinum based chemotherapy is predictive factor of survival after second-line platinum containing chemotherapy (SLPC) in recurrent endometrial cancer.

**Patients and methods:** This study is a multicenter corporative study. We reviewed the clinical data of patients who received SLPC in recurrent endometrial cancer between 2005 and 2009.

**Results:** A total of 265 patients were participated in this study. The median age at the start of SLPC was 63 years old (range 37 to 86 years old). The distribution of initial stage was I, 30; II, 23; III, 124; IV, 88. There were 163 endometrioid adenocarcinoma (grade 1, 41; grade 2, 64; grade 3, 48; not determined, 10), 33 serous adenocarcinoma, 16 clear cell adenocarcinoma, 36 carcinosarcoma, 17 others. The response rates to SLPC for patients with PFI of less than 12 months and 12 months or more were 31.3 and 63.7%, respectively ($p < 0.0001$). The median progression free survival after SLPC for patients with PFI of less than 12 months and 12 months or more were 13.1 (95%CI: 10.4 - 17.4) months and 30.7 (95%CI: 24.9-54.1) months, respectively (hazard ratio; 0.449 (95% CI: 0.311-0.648), $p < 0.0001$).

**Conclusions:** Patients with PFI of more than 12 months had significantly longer survival after SLPC. PFI is predictive factor of response to SLPC and survival after SLPC in recurrent endometrial cancer.
Poster Session III

TO STAGE OR NOT TO STAGE, THAT IS THE QUESTION-OUTCOMES IN ENDOMETRIAL CANCER PATIENTS TREATED SOLELY WITH VAULT BRACHYTHERAPY

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Aims: Assuming that adjuvant vaginal brachytherapy (AVBT) alone is adequate radiotherapy for high-intermediate risk endometrial cancer patients; the aim of this study was to investigate the patterns of failure, survival and salvage for patients who had AVBT alone and to compare the outcomes of those surgically-staged, node-negative patients to those who were deemed not to require lymphadenectomy. The hypothesis being that no difference exists between the two thus validating the surgical criteria for avoiding lymphadenectomy used by our Centre.

Methods: Prospectively collected data on 256 stage I-III, endometrial cancer patients treated with AVBT alone after surgery with or without lymphadenectomy were analyzed for RFS, OS, patterns of failure, and salvage rate.

Results: Median follow-up was 81.7 months. Lymph node staging was performed in 70% with the median number of nodes removed equal to 12. Median time to failure was 21 months. On multivariate analysis for RFS, depth of myometrial invasion was significant, with each mm increasing the relapse risk relapse by 5% (p=0.023). LVSI increased the risk of relapse 3-fold (p=0.002). Multivariate analysis for OS revealed age and LVSI to be significant factors. Lymphadenectomy had no influence on survival. There were 34 failures. Multi-site recurrences occurred in 20 (59%) and 9 (26%) had only distant failures. Isolated pelvic and para-aortic recurrences were 4(12%) and 1(3%) respectively. The salvage rate was one in four.

Conclusions: Surgical nodal staging in this cohort of patients did not improve survival, suggesting that the criteria used intra-operatively adequately assessed the need for lymph node staging.
Poster Session III

LAPAROSCOPIC SURGERY FOR ENDOMETRIAL CARCINOMA: IMMEDIATE RESULTS

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Background, aims & objectives: Laparoscopic treatment for endometrial cancer has gained widespread acceptance. The retrospective study aims to describe our immediate results of laparoscopic surgery for endometrial carcinoma.

Method: The study retrospectively analysed data of 38 consecutive patients (45 yrs to 81 yrs) who underwent laparoscopic surgery for endometrial carcinoma over 18 months (07/2010 to 12/2011). Extent of disease ranged from Stage I to Stage III, Comorbidities included obesity (30/38), Hypertension (32/38), Hypothyroidism (4/38), Coronary Artery Disease (1/38). Total laparoscopic extra fascial hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic lymph node sampling was done. Patients were mobilized the day after surgery.

Results: 1 patient with extensive disease required conversion for cytoreductive surgery and omentectomy. Mortality was nil. Morbidity requiring increased hospital stay beyond 4 days was reduced gut motility (7/38) and respiratory tract infections (4/38). Minor morbidities included electrolyte imbalance, urinary tract infections (3/38), and minor wound infections. Difficulty increasing operating time was encountered in patients with bulky fibroid uterus. There were no major intraoperative injuries. Histopathological evaluation revealed Uterine serous papillary carcinoma (2/38), carcinosarcoma (2/38), clear cell carcinoma (1/38), endometrial stromal sarcoma (1/38), poorly differentiated carcinoma (8/38), and well to moderately differentiated carcinoma (24/38).

Conclusion: Laparoscopic surgery for endometrial carcinoma is a feasible and safe option even in high risk patients. Added benefits are early mobilization, no major issues of wound infection and a reasonably short learning curve especially for surgeons experienced at open surgery.
Poster Session III

PATHOLOGIC FINDINGS AFFECTING POST-OPERATIVE THERAPY OF PATIENTS WITH GRADE 1 ENDOMETRIAL CARCINOMA IN A COMPREHENSIVE SURGICALLY STAGED POPULATION

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Objective: To determine the prevalence of adverse features (deep myometrial invasion [DMI], lymph-vascular space invasion [LVSI], and nodal metastasis [NM]) affecting adjuvant treatment in patients with grade 1 endometrial cancer [G1EC] after extended surgical staging ([ESS]: hysterectomy, bilateral salpingo-oophorectomy, lymphadenectomy [LND]).

Design: 52 patients with G1EC underwent ESS at our center from 2009 to 2011. Clinical and pathologic data were analyzed.

Results: Mean age was 56 (35-78). Mean BMI was 44 (20-61). Mean follow up 24 months (6-36). Surgeries were robotic, vaginal/laparoscopic, open in 71%, 7% and 22%, respectively. Stage distribution was 81%, 13% and 6% in 1A, 1B and 3C, respectively. 17% had DMI, 17% had LVSI. 13% had DMI and LVSI (intermediate risk) and were treated with brachytherapy. 6% had NM requiring additional chemotherapy (CT) and radiotherapy (RT). 7% recurred in the vagina or lymph nodes and were treated with a combination of surgery, CT+/- RT. All patients are alive to date. Accuracy of frozen section for grade was 88%. Mean number of nodes was 26 (10-58), mean length of stay was 1.4 ( 1-7) days. Total operative time for LND was 42 minutes (25-70). The most common complication of LND was lymphocyst (6% with 2 % requiring treatment) and lymphedema (1%).

Conclusion: A significant number of patients (19%) with G1EC after ESS, have adverse prognostic factors influencing postoperative adjuvant treatment. ESS identified 6% with microscopic NM in G1EC. ESS significantly impacts post-operative treatment of G1EC and requires further research.
Poster Session III

IMPACT OF METFORMIN USE IN ENDOMETRIAL ADENOCARCINOMA

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Objective: To evaluate the potential effects of daily metformin use on grade and stage of diabetic patients with endometrial endometrioid adenocarcinoma (EC).

Methods: Patients who underwent full staging procedure with histologically confirmed EC from 2008-2012 were reviewed. Information regarding the amount of antidiabetic medications used, grade, stage of endometrial cancer and comorbid conditions were collected. Differences between baseline characteristics and outcomes of diabetic and nondiabetic patients were assessed with Chi-squared, t-test, and logistic regression. Non-endometrioid histologies were excluded from analysis.

Results: A total of 17 diabetic and 72 nondiabetic patients were identified with mean age of diagnosis 65.5±10.3 and 60.4±12.0 years, respectively. As expected, diabetic patients had a greater use of insulin, statins and higher rates of hypercholesterolemia (p< 0.05) than nondiabetic patients, irrespective of BMI. There was no difference between diabetics and nondiabetics with respect to grade or stage (p>0.05). Though not reaching statistical significance, a trend was observed for lower grade carcinoma with a higher daily cumulative metformin dose (1450g/day for grade 1, 1250g/day for grade 2, and 1050g/day for grade 3).

Conclusion: In vitro studies show that metformin inhibits growth of EC cells. Though metformin was not shown to have any correlation with stage of EC in this study, there may be an association of lower grade with higher daily doses of metformin. A larger powered study is needed to further evaluate this association.
Poster Session III

SHOULD WE RESECT ALL ENDOMETRIAL POLYPS AFTER 40 YEARS OLD?

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**Purpose:** The aim of this study is to determine whether all endometrial polyps should be resected in women 40 years or older.

**Material and method:** 61 patients were resected with a diagnosis of endometrial polyp by hysteroscopy between 2004 to 2012 (Group A). 29 patients were followed up without resection with a diagnosis of endometrial polyp by hysteroscopy between 2010 to 2012 (Group B).

**Results:** There were 2 cancers, 3 atypical endometrial hyperplasia, 1 atypical polypoid adenomyoma, 5 endometrial hyperplasia, 42 endometrial polyp and 8 benign endometrium in 61 patients treated by resection. In 6 patients with atypical hyperplasia or endometrial cancer, all were diagnosed suspicious by endometrial cytology and/or MR imaging before treatment, and abnormal genital bleeding were seen in 5 of these 6 patients. Among 12 patients with suspicious by endometrial cytology, 9 patients were diagnosed benign endometrial polyp by hysteroscopy. In these 9 patients, final diagnoses were 8 endometrial polyps and 1 atypical endometrial hyperplasia. On the other hand, 29 patients in group B, whose cytology were 5 suspicious and 24 normal, became normal during follow up.

**Conclusion:** In case of endometrial polyp, hysteroscopy is very useful for diagnosis of endometrial polyp and decision the necessity of resection. In cases of repeated abnormality of cytology or some abnormal findings by hysteroscopy, these polyps should be resected. If a diagnosis of benign endometrial polyp is provided by hysteroscopy, follow-up is possible without resection.
Poster Session III

EIGHTEEN CASES OF GYNECOLOGICAL CANCER AFTER BREAST CANCER

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Objectives: It is well known that there was an association between breast cancer and endometrial cancer or ovarian cancer for the hormonal treatment and genetic connection. We tried to show the effect of gynecological follow-up after breast cancer, since we had done gynecological cancer screening for the patients with breast cancer hormonal treatment.

Methods: We collected medical records data from 1996 to 2010 retrospectively. We determined gynecological cancer as endometrial, ovarian and cervical cancer, uterine and ovarian carcinosarcoma. We recognized 18 cases had gynecological cancer after breast cancer respectively.

Results: There were 7 cases of uterine endometrial cancer, 3 cases of cervical cancer, 3 cases of uterine carcinosarcoma, 4 cases of ovarian cancer and 1 case of ovarian carcinosarcoma. The median age diagnosed breast cancer was 55 (40-66) years old. While 6 patients of 7 endometrial cancer patients had taken tamoxifen, only 3 cases were diagnosed during the follow-up period. 5 cases of total 18 cases were diagnosed gynecological cancer by the gynecological screening during the follow-up period, 10 cases were diagnosed from atypical genital bleeding, 3 cases were from abdominal symptom. The median age diagnosed gynecological cancer was 61.5(42-73). The duration from the time when patients were diagnosed breast cancer to when the patients were diagnosed gynecological cancer was 66 months(24-220).

Conclusions: Only 6 cases had been diagnosed gynecological cancer from gynecological cancer screening during breast cancer hormonal treatment. Most of cases were diagnosed after follow-up term. The cancer screening after breast cancer had limited value.
LYMPHADENECTOMY IN ENDOMETRIOID ENDOMETRIAL CARCINOMA WITH INNER HALF MYOMETRIAL INVASION

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Objective: To determine the incidence of lymph node metastasis (LNM) and identify factors associated with LNM in endometrioid endometrial carcinoma with inner half myometrial invasion.

Methods: Patients with endometrioid endometrial adenocarcinoma with inner half myometrial invasion who underwent surgical staging including lymphadenectomy between January 2002 and March 2012 were retrospectively reviewed. Pelvic lymphadenectomy was performed in all patients, and patients with grossly enlarged lymph nodes underwent paraaortic lymphadenectomy.

Results: Of the 95 patients (ages 34-75 years), 7 (7%; ages 41-60 years) had LNM. All 7 patients (7%) had pelvic LNM, and one (1%) had paraaortic LNM. LNM was observed in 2 of 52 (4%) Grade 1, 4 of 35 (11%) Grade 2, and 1 of 8 (13%) Grade 3 diseases. Patients aged ≤55 years were more likely to have LNM than those aged ≥56 years (6/42 [14%] vs 1/53 [2%), P < 0.05). Lymph node swelling was detected on preoperative imaging studies in 2 patients, including 1 patient with paraaortic LNM. Of 5 patients without lymph node swelling on preoperative imaging studies, 1 had an elevated CA-125 level, and 1 had enlarged lymph nodes detected intraoperatively; however, 3 other patients, who were aged ≤55 years, had none of these two findings.

Conclusion: LNM is not rare in endometrioid endometrial carcinoma with inner half myometrial invasion, and most LNM occurs in the pelvic region. Patients aged ≤55 years may benefit from pelvic lymphadenectomy, even if they have a normal CA-125 level and no lymph node swelling is detected on preoperative imaging studies.
Poster Session III

RETROSPECTIVE STUDY OF ENDOMETRIAL CANCER RECURRENCE AT LANCASHIRE AND SOUTH CUMBRIA CANCER NETWORK


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Background: Endometrial cancer is the most common gynaecological malignancy, and is traditionally treated with surgery and adjuvant radiotherapy. Recurrence rates are low and the vast majority are symptomatic at presentation. Current guidance dictates 5-year clinic based surveillance of variable frequency.

Aim: To examine the mode of presentation and to evaluate the role of routine clinic follow ups in the detection of recurrent endometrial cancers and to assess the possible impact of early discharge within the national 'survivorship' initiative.

Methods: Retrospective review of case notes of patients with recurrent endometrial cancers.

Results: 78 patients were identified to have recurrent endometrial cancer during the study period (April 2006 - July 2011). The mean age of diagnosis and recurrence was 67.4 and 70.1 years, respectively. The mean duration from initial treatment to recurrence was 33.7 months with only 55% been diagnosed within 2 years of follow up. 85% of the recurrences occurred within 5 years follow up period. Majority of the endometrial cancer recurrences had symptoms (88%) and clinical examinations at routine follow up clinics only detected few asymptomatic recurrences (12%). About half the patients with symptomatic recurrences reported their symptoms to their GP or emergency services between follow-up visits.

Conclusion: Post-operative hospital based follow-up is responsible for detecting only a small number of asymptomatic recurrences. The majority of patients presented with symptoms via A&E or General Practice, which brings into question the role of interval follow up in these patients.
INVITRO TOLUIDINE BLUE APPLICATION IN THE DIAGNOSIS OF ENDOMETRIYAL PATHOLOGIES

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Objectives: The aim of this study was to assess the usefulness of toluidine blue staining in the evaluation of endometrial premalign or malign lesions especially in locating the sampling area during a frozen section procedure.

Methods: 106 patients were planned to have hysterectomy. The study group was consisted of 53 patients, of whom, 14 of them were operated due to simple endometrial hyperplasia, 12 of them due to endometrial hyperplasia with complex atypia and 27 of them due to endometrial cancer confirmed by preoperative hysteroscopic biopsies. The control group (n: 53) was formed with patients who were operated with a diagnosis of leiomyoma. The preoperative endometrial samplings of the control group were all reported as non-neoplastic endometriyum. All uterine specimens were stained with toluidine blue, immediately at the operation room, than sent to frozen section procedure.

Results: The sensitivity of toluidine blue in the determination of endometrial pathologies was 100% with a specificity of 94%. The positive predictive value of toluidine blue in the staining of endometrium as a diagnostic test was 94% with a negative predictive value of 100%. Positive LR: 18.6 (95%CI 6.20-56.12).

Conclusions: Our results showed that toluidine blue staining of endometrium is a reliable, new technique and may be used in frozen section procedure with high sensitivity if an uterine malignancy is suspected. In addition its use in office hysteroscopy (Chromohysteroscopy) will be an important step in the evaluation of endometrial pathologies where will be introduced in further trials.
Poster Session III

THE MANAGEMENT OF ENDOMETRIAL CANCER IN MORBIDLY OBESE WOMEN: IDENTIFYING BEST PRACTICE

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Objective: The incidence of Endometrial Carcinoma (EC) is set to increase with the escalating global epidemic of obesity. Management of these patients poses difficulties as they often have comorbidities sufficient to exclude surgery and are at an increased risk of postoperative complications. We sought to compare local and national practice in the management of these patients and attain a gold standard of care.

Methods: The Somerset Cancer Register identified 175 patients diagnosed and treated for EC from April 2010 to March 2011 at Liverpool Women's Hospital. A retrospective search of the case notes for thirty-one morbidly obese patients was completed. A national survey was distributed to the major Cancer Centres in the UK to establish current practice.

Results: Of the 17.7% (31/175) morbidly obese patients twenty-five underwent surgical management and six medical. 60% (15/25) had a total hysterectomy with bilateral salpingo-oophorectomy (TAH BSO), with or without pelvic and para-aortic lymphadenectomy. The remainder underwent vaginal hysterectomy or laparoscopic assisted vaginal hysterectomy and BSO. Medroxyprogesterone acetate was the mainstay of medical management with adjuvant radiotherapy in appropriate candidates. 48% (12/25) suffered postoperative complications ranging from wound infection to pulmonary embolus, all of these in the TAH BSO cohort.

Conclusion: Morbidly obese patients with EC are at increased risk of death from all causes, including postoperative complications. Minimally invasive surgery offers the chance of reducing morbidity and mortality, but is technically very difficult and requires experienced surgeons. The longterm safety of laparoscopic approaches remains to be tested in prospective randomised trials.
Poster Session III

MRI GUIDED SALVAGE HIGH DOSE RATE (HDR) INTERSTITIAL GYNECOLOGICAL BRACHYTHERAPY

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Purpose: To document single institutional experience in Salvage Gynecological HDR Interstitial brachytherapy.

Methods: An institutional ethics approved prospective brachytherapy database was created. Forty-three cases of recurrent gynecological cancers were treated between Jan 2003 to Dec 2011. Twenty-three (64%) patients had uterine, 7 (19%) had cervical, 5 (14%) had vaginal metastasis from a GU/GI primary and 1 (3%) had vulvar cancer. Thirty-four (94%) cases had prior hysterectomy and were divided into Group 1 no prior radiotherapy (n=24) and Group 2 re-irradiation (n=12). Thirty three (77%) were treated with a combination of external beam (4500cGy/25) followed by brachytherapy boost. Ten (23%) received brachytherapy alone. Median brachytherapy dose was 650 cGy (range 550-700). All patients had CT/MRI image guided radiation therapy planning.

Results: Median follow-up 52.5 months (range: 15 -196). Overall 23 (64%) patients are disease free (16(70%) in Group 1 and 7 (30%) in Group 2). Median time to relapse is 53 months (range: 12-182). Eight (33%), 4 (33%) patients from Group 1 and 2 respectively relapsed and died of their cancer. Central recurrence and distant relapse was 6(25%) and 5 (21%) in Group 1; 4 (33%) and 3 (25%) in Group 2. There was no difference in survival in both the groups (p=0.530). One patient from Group 2 developed late RTOG Grade 4 GI toxicity that required surgical intervention. No late GU toxicity was seen in either group.

Conclusions: Good local control can be achieved with combination of external beam and salvage image guided HDR interstitial brachytherapy in carefully selected cases.
Poster Session III

ENDOMETRIAL ADENOCARCINOMA IN PATIENTS WITH LYNCH SYNDROME: CLINICAL FACTORS AND SURVIVAL IN BRAZILIAN WOMEN

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Background and aims: Lynch syndrome is associated with colorectal cancer and other extra-colonic cancers. In women, endometrial cancer is the most common cancer. The aims are to estimate the percentage of patients at risk for Lynch syndrome and to compare the survival of patients with and without risk of Lynch syndrome (groups 1 and 2).

Patients and methods: Consecutive patients with endometrial carcinoma with endometrioid histology who underwent primary surgical treatment. The criteria used to assess the risk of Lynch syndrome were the Amsterdam II criteria, modified Bethesda guidelines, endometrial cancer before age 50 and first-degree relative with Lynch syndrome-associated tumor. The study was approved by the Research Ethics Committee of Universidade Federal de Ciencias da Saude de Porto Alegre and of Hospital de Clinicas de Porto Alegre.

Results: Twenty-eight (25.2%) of the 111 patients had clinical criteria and/or suspicion of Lynch syndrome (group 1). The survival at two and five years in group 1 (Lynch syndrome) was 95.8% and 90.5%, respectively, and in group 2 (probably sporadic cases), 87.6% and 78.9% (P=0.11).

Conclusions: The frequency of patients at-risk for Lynch syndrome was higher than expected, and the survival rate of patients with endometrial carcinoma and clinical history suggestive of Lynch syndrome was better (but not significant) than those with sporadic tumors, although no difference in staging between the groups was observed. This is the first study that presents a combined evaluation of the frequency of the Lynch syndrome phenotype and survival rates of Brazilian women with endometrial carcinoma.
Poster Session III

ENDOMETRIAL ADENOCARCINOMA IN PATIENTS WITH RISK LYNCH SYNDROME: IMMUNOHISTOCHEMISTRY FOR P53 PROTEIN AND MLH1, MSH2, MSH6 AND PMS2 PROTEINS

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Aims: To evaluate the expression of p53 in groups 1 and 2 (Lynch syndrome and sporadic) and to identify the expression of proteins mlh1, msh2, msh6 and pms2.

Patients and methods: Patients with endometrial carcinoma. IHC was used for screening of Lynch syndrome in patients at risk and IHC analyses for identification of the p53 protein in all patients. The study was approved by the Research Ethics Committee of Universidade Federal de Ciencias da Saude de Porto Alegre and of Hospital de Clinicas de Porto Alegre.

Results: The expression of p53 in groups 1 and 2 was 34.8% and 51.9% (P = 0.06). In eleven (25.6%), the results showed loss of expression of MMR proteins. Two cases showed loss of mlh1, two cases showed loss of msh2, three cases showed loss of msh6, and three cases showed loss of pms2 expression. Simultaneous loss of mlh1 and msh6 expression was observed in one case. Among 32 patients with suspected Lynch syndrome and normal expression of MMR proteins, six (two under 50 years) had families meeting the Amsterdam criteria, 14 (three under 50 years) had families meeting the Bethesda guidelines, nine were younger than 50 years and three had a first-degree relative with Lynch syndrome-related tumor.

Conclusions: Lynch-syndrome tumors showed a lower rate of p53 expression than sporadic tumors, with a borderline significant difference. The valid percentage of IHC results suggestive of Lynch syndrome among the suspected cases was 25.6% (11/43).
Poster Session III

PREVALENCE OF ABNORMAL MISMATCH REPAIR PROTEIN EXPRESSION IN HIGH-GRADE ENDOMETRIAL CARCINOMA: A CLINICOPATHOLOGIC STUDY

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Introduction: There are no accepted guidelines regarding which endometrial carcinoma (EC) patients should undergo testing for Lynch syndrome by mismatch repair (MMR) protein immunohistochemistry (IHC). The prevalence of abnormal MMR expression in high-grade EC has not been described.

Objectives: To assess the prevalence of expression of common MMR proteins in our cohort of high-grade EC. To determine demographic/clinical differences in our cohort stratified according to MMR status.

Methods: From a cohort of 116 cases of high-grade EC treated at our institution between 2005-2011, a consolidated consensus diagnosis was derived in 99 cases by a combination of re-review with IHC markers. Tissue microarrays were stained for MLH1, PMS2, MLH2, and MSH6 using two conventional IHC platforms and AQUA HistoRX immunofluorescence. Slides were scored by 2 observers and consensus was reached in discrepant cases using the most sensitive assay. Demographic and clinical data was extracted and stratified according to MMR status.

Results: Any abnormal MMR expression was observed in 32% of cases, which was different across histological types: dedifferentiated carcinoma (80%), FIGO grade 3 EC (45%), clear cell carcinoma (18%), and serous carcinoma (0%). The abnormal marker distribution was PMS2 (28%), MLH1 (23%), MSH6 (5%) and MSH2 (0%). The 4/54 patients with FIGO grade 3 EC and loss of MSH6 were not significantly younger.

Conclusion: Endometrial serous carcinomas do not show abnormal MMR IHC and can be spared from testing. The role of MSH6 IHC testing in older patients with FIGO grade 3 EC warrants further study.
Poster Session III

RETROSPECTIVE ANALYSIS OF STAGE IC UTERINE CARCINOMA PATIENTS

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Background: Stage IC patients are at an increased risk of recurrence and overall worse prognosis compared with stage IA and IB patients. The objective of this study is to evaluate treatment outcomes at a single institution in patients with 1988 FIGO stage IC endometrial adenocarcinoma.

Methods: Records of the patients with FIGO stage IB (formerly IC) endometrial cancer were retrospectively evaluated. All patients were initially treated surgically with comprehensive staging lymphadenectomy.

Results: Totally 85 patients were included. Median age of the patients was 60 (range 27-95). Fifty-nine patients had at least one co-morbid disease. Complete surgical staging including pelvic and paraaortic lymph node dissection was performed in all the patients. Sixteen patients (19%) received adjuvant chemotherapy, including 6 patients with serous cancer and one patient with small cell cancer. Paclitaxel/carboplatin was the preferred regimen in Median follow up was 30 months (range 10-61 months). Seven patients (8%) relapsed and 4 patients (5%) died on follow up. 5 year disease free survival was 89% and overall survival was 95%. One of the 16 patients (6.2%) who received chemotherapy and 6 of the 69 patients (8.7%) who did not receive relapsed/died on follow up.

Conclusions: We found similar rates of recurrence and death with previous studies in stage IC endometrial cancer. Complete surgical staging is the mainstay of treatment. Marginally lower recurrence rate in chemotherapy treated patients delineate the need for prospective randomized data addressing the role of adjuvant systemic therapy in early-stage patients with endometrial adenocarcinoma.
Poster Session III

RETROSPECTIVE ANALYSIS OF STAGE III UTERINE CARCINOMA PATIENTS: A SINGLE CENTER EXPERIENCE

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Background: Stage IIIC comprises 8% of all endometrial cancers. Both local and systemic relapse risks are high. We herein report outcomes of our patients with stage IIIC endometrial cancer.

Methods: 29 patients with stage IIIC endometrial cancer diagnosed between 2006-2011 were included.

Results: Median age was 64 (41-82). Surgical procedure was TAH+BSO+BPPLND and omentectomy in 26 patients. 4 patients who were operated (TAH+BSO) in another center were restaged and BPPLND and omentectomy were performed. 13 patients (45%) had endometrioid histology, 11 (38%) had papillary serous carcinoma, 2 (7%) had clear cell carcinoma, 2 (7%) had mixed carcinoma and 1 (3%) had undifferentiated carcinoma. 14 patients (48%) had positive nodes both in pelvic and paraaortic region, 9 (31%) only in pelvic region and 6 (21%) only in paraaortic region. 24 patients (83%) received chemotherapy with paclitaxel and carboplatin, 13 (45%) received external RT, 4 (14%) received brachytherapy and 3 (10%) patients received chemoradiation with weekly cisplatin or carboplatin. Median follow up was 19 months. 10 patients recurred during follow-up and 6 patients died. 3-year PFS was 64% and OS was 71.6%.

Conclusions: With the use contemporary chemotherapy regimens and radiotherapy, we achieved ~70% 3-year survival rate in stage IIIC endometrial carcinoma patients with 45% of the patients having high risk histologies (serous and clear cell). We propose that combined adjuvant chemotherapy and radiation might improve survival in patients with advanced stage disease compared to either modality alone. Results of GOG258 and PORTEC 3 trials should be awaited for definitive conclusions.
Poster Session III

STAGE I PAPILLARY SEROUS AND CLEAR CELL UTERINE CARCINOMA: SINGLE CENTER EXPERIENCE

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Background: Uterine clear cell and papillary serous carcinoma are uncommon but aggressive types of endometrial carcinoma with high recurrence rate and poor survival outcomes, even with apparent early stage disease. 5-year overall survival rates range from 50% to 80%. The purpose of this study was to determine the patterns of recurrence and survival outcomes in patients with surgical stage I clear cell and papillary serous carcinoma treated with platinum based chemotherapy.

Methods: Records of the patients with FIGO stage I serous papillary or clear cell endometrial cancer were retrospectively evaluated. All patients were initially treated surgically by the same surgeon with comprehensive staging lymphadenectomy, i.e. total abdominal hysterectomy, bilateral salpingooopherectomy, bilateral pelvic and paraaortic lymph node dissection and omentectomy.

Results: Sixteen patients included in this study. 13 patients(81%) had serous papillary, 3 patients had clear cell carcinoma. Median age was 62 and 94% of the patients were post menopausal. Thirteen patients received chemotherapy with paclitaxel and carboplatin for 6 cycles. One patient died postoperatively without receiving any adjuvant treatment, one received radiotherapy and 3 received brachytherapy. Median follow up was 15 mos. Only one patient died on follow up because of cardiac etiology and the remaining 15 are alive and disease-free.

Conclusions: Complete surgical staging and adjuvant chemotherapy results in excellent prognosis in our patient series, although follow up period is relatively short.
Poster Session III

FINAL RESULTS OF A LARGE INTERNATIONAL ANALYSIS OF THE IMPACT OF L1-CAM EXPRESSION IN FIGO STAGE I, TYPE-1 ENDOMETRIAL CANCER


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Aims: Although, endometrial cancer, especially when diagnosed in FIGO stage I exhibits excellent prognosis, a significant number of patients develop early recurrence. This multicenter study was performed to investigate the impact of expression of the neural cell adhesion molecule L1-CAM (CD171), even in small tumor areas, to identify early endometrial cancers with such a particular aggressive behavior.

Methods: L1-CAM expression was immunohistochemically assessed in 1031 endometrial cancers and correlated with clinicopathologic parameters and outcome. For this purpose the monoclonal mouse antibody L1 clone-14.10 [Covance, Princeton, NJ] was used on paraffin embedded specimens. L1-CAM positivity was defined as ≥ 5% of positive cells or circumscribed L1-CAM expressing islets. Blinded evaluation of the specimens was done by two independent pathologists.

Results: 18.3% of the investigated cancers were found to be L1-CAM positive. Based on risk assessment L1-CAM positivity rate was significantly higher in the intermediate/high risk cancers (27.8%) compared to the low risk cancer group (13%). In addition, L1-CAM positivity correlated with histopathological grading (p=0.0001) and increasing depth of myometrium infiltration (p=0.027). 11.6% of patients experienced recurrence, whereby recurrences occurred significantly more frequently in L1-CAM positive tumors (p=0.0001). In the Cox model L1-CAM expression retained independent prognostic significance with an impressive odds ratio of 21.74 (13.49-35.03) for recurrence and 13.29 (8.47-20.88) for overall survival.

Conclusions: L1-CAM positivity in stage I, type 1 endometrial cancers reliably identifies a subset of cancers with very high risk for recurrence and poor survival. These cancers are candidates for trials evaluating the value of adjuvant treatment, and in addition, L1-CAM expression may contribute as a novel tool to therapeutic decision-making.
Poster Session III

FREQUENCY OF ENDOMETRIAL CANCER IN WOMEN AT HIGH-RISK FOR PELVIC SEROUS CARCINOMA: WHAT ABOUT THE UTERUS?

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Background: Serous endometrial intraepithelial carcinoma (SEIC) has been proposed to be a potential precursor lesion of pelvic serous carcinoma. If true, an increased frequency of uterine papillary serous carcinomas would be expected in women at high-risk of developing pelvic serous carcinoma.

Objective: This study explored particularly the occurrence of uterine papillary serous carcinoma, as well as other endometrial cancers, following risk-reducing salpingo-oophorectomy (RRSO) in women with a hereditary or familial increased risk of developing pelvic high-grade serous carcinoma attending a tertiary multidisciplinary clinic.

Methods: Consecutive women with a deleterious BRCA1/2-mutation and women from a hereditary ovarian cancer family who had undergone RRSO without hysterectomy at the University Medical Center Groningen from January 1996 until January 2012 were followed prospectively. They were crossed with the list of endometrial cancer diagnoses reported by the Dutch nation-wide pathology database PALGA.

Results: Overall, 380 women at a median age of 50.0 years (range, 31-77) were analyzed. After a median follow-up of 5.0 years after RRSO, two cases of endometrial cancer were diagnosed, whereas the expected was 0.56 cases. Both were of the endometrioid histological subtype and no uterine papillary serous carcinomas were diagnosed, and they did not use tamoxifen in the past. The endometrial cancer risk was not significantly elevated (SIR 3.56, p=0.06).

Conclusion: We show that the incidence of post-RRSO endometrial cancer in women at high-risk of developing pelvic serous carcinoma is as expected. Based on our in-house data, the hypothesis of SEIC being the precursor lesion of pelvic serous carcinoma seems unlikely.
Poster Session III

THE PREVALENCE OF DISTANT METASTASIS IN HIGH GRADE ENDOMETRIAL CANCER PATIENTS

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Background: Most patients with endometrial cancer have a favourable prognosis. Yet, about 25% present with high grade tumours associated with a risk of extended disease and recurrence. Primary treatment consists of hysterectomy and bilateral salpingo-oophorectomy (BSO). Lymphadenectomy and omentectomy is recommended for non-endometrioid type endometrial tumours. There is no consensus for lymphadenectomy for high grade endometrioid tumours nor for the type of adjuvant treatment for high grade tumours. Currently, adjuvant radiotherapy is recommended if ≥ 2 risk factors are present (i.e. deep myometrial invasion, age > 60, high grade), or include patients in the PORTEC 3 trial.

Methods: All patients (n=239) diagnosed with high grade endometrial cancers at the Comprehensive Cancer Center South (CCCS) between January 2005 and December 2011 were included. Data of patient, and tumour characteristics, primary and adjuvant treatment, and outcome were extracted from the ROGY database.

Results: Preliminary results of the first 87 included patients: grade 3 endometriod type 66% (n=57), papillary serous 28%(n=24), clear cell type 7%(n=6).

All early stage patients (n=52) underwent hysterectomy and BSO, only 23% (n=12) underwent a lymphadenectomy. Adjuvant radiotherapy was recommended for 98,1% (n=51) while actual 29 (55.8%) received adjuvant radiotherapy. The recurrence rate in the radiotherapy group was significantly lower (17.2% vs. 39.1%). However, in case of recurrence, distant metastasis was very common (80% vs. 77.8%).

Conclusion: Adjuvant radiotherapy in all high grade endometrial tumours reduces the risk of recurrences. High frequency of distant metastasis suggests the use of systemic adjuvant therapy even in early stage disease.
Poster Session III

ENDOMETRIOID ADENOCARCINOMA ARISING FROM ADENOMYOSIS IN A 67 YEAR-OLD PATIENT: A CASE REPORT

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Adenomyosis is a common pathologic condition of the uterus which has the potential for malignant transformation. Adenocarcinoma arising from adenomyotic foci is considered a rare occurrence. Adenomyotic foci have substantial growth potential and the downward extensions of the basal layer of the endometrium can undergo malignant transformation. When persistent estrogenic stimulation is present, proliferative changes may occur in these foci, including hyperplastic changes that can develop into carcinoma. We report a case of a 67 year old woman with postoperative findings of a poorly differentiated primary endometrioid adenocarcinoma arising from adenomyosis without endometrial involvement. Immunohistochemical staining with CK7, CK20, estrogen (ER), progesterone (PR), and Wilm's tumor 1 (WT1) receptors confirmed the diagnosis. The patient underwent post-operative double-agent chemotherapy and is without clinical evidence of disease.
Poster Session III

PURE VERSUS MIXED SEROUS ENDOMETRIAL CARCINOMA: TWO DIFFERENT ENTITIES?

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Objective: To determine whether the percentage of UPSC histology impacts upon clinical outcomes and to identify clinicopathologic prognostic factors predictive for recurrence and survival in stage I-IV UPSC patients. Furthermore, we assessed UPSC for their association with the precursor lesion endometrial intraepithelial carcinoma (EIC).

Methods: A retrospective multi-institution analysis of stage I-IV UPSC patients was performed. All histopathological slides were reviewed systematically and independently by four expert pathologists, with determination of the percentage UPSC histology within each tumor.

Results: We identified 108 UPSC patients. Fifty-eight patients had mixed UPSC histology (53.7%), and 50 patients (46.3%) had pure UPSC. On multivariable analysis, advanced FIGO stage, mixed UPSC histology, and LVSI were significantly associated with recurrence. Furthermore, FIGO stage and the percentage UPSC histology were significantly and independently associated with both PFS and OS. The precursor lesion EIC was identified in 78 out of 93 patients (83.9%), with no significant difference among mixed and pure UPSC patients. Atrophic/weakly proliferative endometrium was found in 90.7% of pure UPSC cases, whereas hyperplastic endometrium with atypia was more commonly found in 34.7% of mixed UPSC patients ($p = 0.004$).

Conclusion: The percentage UPSC histology and FIGO stage are the most important prognostic risk factors for recurrence and survival in stage I-IV UPSC. Further, the precursor lesion EIC was equally found among both pure and mixed UPSC cases, whereas the non-neoplastic endometrium was atrophic/weakly proliferative in pure UPSC cases compared to more hyperplastic with atypia in mixed UPSC cases.
INCIDENTAL DIAGNOSIS OF ENDOMETRIAL CANCER DURING THE UK FAMILIAL OVARIAN CANCER SCREENING STUDY (UKFOCSS)

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Background: Women at high risk of ovarian cancer (OC) may be at increased risk of endometrial cancer (EC). We wanted to establish whether women on UKFOCSS had developed EC, and if so, whether it was diagnosed by the OC screening protocol.

Methods: Women (all >35yr old) underwent TVS initially annually and subsequently more frequently if CA125 levels were high/rising using a risk of OC algorithm (ROCA). We identified those with abnormal endometrial morphology or thickness (≥5mm if postmenopausal) on TVS, and/or diagnosed with EC.

Results: 453 (8%) of 5732 women were referred for an incidental abnormal endometrial finding. 10 (2%) of these had EC, of which 70% were FIGO stage 1a or 1b. 11 women had interval EC diagnosed via clinical presentation. 10/21 (48%) EC cases were premenopausal, of which 5 (50%) had Lynch Syndrome. Overall EC detection sensitivity, specificity, PPV and NPV were 48% (95% CI 28-68), 92% (CI 91-93), 2% (CI 1-4) and 99.8% (CI 99.6-99.9), respectively. Sensitivities in premenopausal and postmenopausal women were 20% (CI 25-55) and 73% (CI 39-94) respectively. 10/17 cases in whom the ROCA was used had non-normal results at diagnosis.

Conclusions: Participants had a 1 in 12 chance of referral for an incidental endometrial abnormality. 1 in 50 women with abnormal endometrial findings had EC, so referral in this population was warranted. Overall EC detection sensitivity and PPV were low, reflecting poor performance of ultrasound screening in the premenopausal population. EC diagnosis may be associated with a rising pattern of CA125.
Poster Session III

PEGYLATED LIPOSOMAL DOXORUBICIN (PLD) AND CARBOPLATIN IN MALIGNANT MIXED EPITHELIAL MESENCHYMAL AND MESENCHYMAL GYNECOLOGIC TUMORS: A META-ANALYSIS AGO STUDY-GROUP TRIALS


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Background: After conduction of a pure gynecologic sarcoma trial (AGO-GYN7) showing promising activity of PLD and carboplatin we performed a meta-analysis including two other trials in whom patients with gynecologic sarcomas were treated with the same regimen.

Methods: Patients with advanced or recurrent gynecologic sarcoma or carcinosarcoma treated within the AGO-GYN2 or AGO-GYN3 or AGO-GYN7 trial were analysed. AGO-GYN2 was a dose-finding phaseI/II trial (PLD 20 to 50mg and carboplatin AUC6). The two other trials investigated PLD 40mg/m² and carboplatin AUC6,q28.

Results: The study group comprised 59 patients: 30 pts. with carcinosarcoma, 20 pts. with leiomyosarcoma and 9 pts. with endometrial stroma sarcoma. 93% of the patients had primary diagnosis. 91.5% of the pts. received PLD 40mg/m² and carboplatin AUC6,q28. The incidence of grade 3/4 hematologic toxicities was anemia 17%, neutropenia 52.6% and thrombocytopenia 23.8%. Febrile neutropenia occurred in one patient. Main grade 3/4 non-hematologic toxicities were: PPE 5.1% and constipation 3.4%. The rate of CR/PR was 31.6% and of CR/PR/SD 68.4% (58.8% in carcinosarcoma, 80% in leiomyosarcoma and 66.7% in endometrial stroma sarcoma). 12months PFS and OS were 38.1% and 74.6%, respectively. Thera was no real difference in PFS and OS realted to the different tumor types.

Conclusions: The combination of PLD and carboplatin is an active regimen in gynecologic sarcomas. The safety profile seems to be favourable compared to other widely used combination therapies for those diseases.

The original studies were supported by Essex Pharma.
Poster Session III

MANAGEMENT OF ENDOMETRIAL CANCER: WHICH TREATMENT-STRATEGIES ARE USED WORLDWIDE? A SURVEY BY THE NORTH-EASTERN-GERMAN SOCIETY OF GYNAECOLOGICAL ONCOLOGY (NOGGO)

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Objective: To assess the therapeutic strategies that are frequently applied in the management of endometrial cancer (EC) on an international level. We conducted an international survey evaluating the current status-quo of systemic, radiotherapeutic and operative management of EC.

Methods: A validated 15-item-questionnaire regarding adjuvant and surgical procedures against EC was sent to all major gynaecological cancer societies and study groups worldwide.

Results: In a phase-I-national trial, the questionnaire was validated on basis of 316 German institutions. On the phase-II-international survey a total of 302 questionnaires were answered from 24 countries, mainly from Japan (38.7%), Spain (8.3%), Austria (7%), United-Kingdom (6.3%), Italy (6%) and USA (4.3%). The vast majority of the participating clinics were academic (62.8%).

For stage I disease with high risk factors (low differentiation, L1,V1) chemotherapy was the first choice of treatment (46.4%), while 36.8% of the clinics decided to use a vaginal brachytherapy. Even for FIGO stage II both therapeutic strategies, vaginal brachytherapy (42.4%) and chemotherapy (39.1%), were commonly used, 34.1% selected external pelvic irradiation. For advanced stage III&IV disease the vast majority (60.3% and 79.5%, respectively) of the physicians indicated systemic chemotherapy alone, or used the combination of irradiation and systemic chemotherapy (49.3% and 35.8%). For the treatment of advanced -stage disease 81.8% of the participants decided to use Paclitaxel+Carboplatin, while Doxorubicin+Cisplatin was chosen by 11.9%.

Conclusions: The clinical management of EC varies worldwide, underlining the need of future prospective randomised trials which will establish standard and evidence based treatment strategies for EC- disease.
Poster Session III

SURGICAL AND SURVIVAL OUTCOMES AFTER COMPREHENSIVE ROBOTIC SURGICAL STAGING FOR ENDOMETRIAL CANCER

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Aims: To assess short- and long-term outcomes after robotic surgery for endometrial cancer staging.

Methods: A prospectively entered oncologic database was queried to identify consecutive patients submitted to robotic surgery for apparently early stage endometrial cancer at a single institution. Robotic approach with a Da Vinci S platform was offered as the first treatment option regardless patient's age, BMI, medical history and anesthesiological risk. Pelvic and aortic lymphadenectomy were performed according to the tumour grade and to the myometrial invasion at the frozen section analysis.

Results: Starting from November 2006, 150 women received comprehensive surgical staging for endometrial cancer. The median (range) age and BMI were 63.4 (31.5-84.2) years and 31.3 (18.5-69.0) kg/m², respectively. Pelvic and aortic lymph nodes retrieved were 20.5 (range 9-70) and 10.5 (range 3-20). Three (2.0%) women required blood transfusion, 1 (0.7%) conversion to laparotomy was required for anesthesiological indication; 2 (1.3%) and 6 (4.0%) patients experienced intra- and post-operative complications, respectively. After a median follow-up of 20.3 (range 4.5-53.9) months, 6 (4.0%) patients had a recurrence and 1 (0.6%) died of disease, whereas 2 (1.3%) women died other unrelated causes.

Conclusions: Robotic surgery represents a viable option to properly perform a comprehensive surgical staging for endometrial cancer with a low complications rate. Longer follow-up is needed to establish definitive conclusions on survival.
Poster Session III

SKIP METASTASIS IN ENDOMETRIAL CANCER

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Objectives: To identify the incidence of patients who have para-aortic lymph node metastasis without pelvic node metastasis and to emphasize the need for systematic pelvic and para-aortic lymph node dissection in all endometrial cancer patients.

Methods: A single centre retrospective analysis was performed including patients treated for endometrial cancer between 2009 and 2012. Over 3 years, 128 consecutive patients were managed by predefined surgical guidelines differentiating low-risk patients from patients at risk for dissemination requiring systematic lymphadenectomy. Low risk was defined as grade 1 endometrioid type with myometrial invasion < 50% and primary tumor diameter < 2 cm.

Results: Hysterectomy was performed by laparoscopically in 13.3% of patients. Lymphadenectomy was not required in 11% of patients (all low risk). 54 patients (42.5%) was found to have only pelvic lymphadenectomy. A total of 59 patients (48.8%) underwent systematic pelvic and para-aortic lymphadenectomy extending to the renal vessels, were studied. 43 of 59 patients had no pelvic lymph node involvement. However 3 of 43 patients without pelvic lymph node metastasis had isolated para-aortic lymph node metastasis (6.98%).

Conclusion: Para-aortic lymph node metastasis in patients without pelvic node involvement (6.98%) is high enough to consider routine pelvic and paraaortic lymphadenectomy in patients with endometrial cancer.
Poster Session III

VALIDITY OF INTRAOPERATIVE EXAMINATION OF MYOMETRIAL INVASION IN PATIENTS WITH ENDOMETRIAL CANCER

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Objectives: Today systematic lymphadenectomy in endometrial cancer (EC) is frequently performed to risk factors for lymph node involvement. Low risk was defined as grade 1 endometrioid type with depth of myometrial invasion (MI) < 50% and primary tumor diameter < 2 cm. We aimed to identify the validity of intra-operative frozen section (FS) examination of MI compared to final histology (FH).

Methods: A retrospective analysis of 128 consecutive patients treated for EC between 2009 and 2012 was performed. Correlation between FS and FH and sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of FS in predicting depth of MI in permanent section were calculated.

Results: Ninety six women (75%) had an endometrioid adenocarcinoma, 4 (3.1%) a serous carcinoma, 6 (4.7%) a clear cell carcinoma, 9 (7%) a mixed type carcinoma and 12 (9.4%) a carcinosarcoma. In 14 of 58 cases who have FS examination of MI < 50%, FH was MI ≥50% (24.1%). In 2 of 47 cases who have FS examination of MI ≥50%, FH was MI < 50% (4.26%). 4 of 9 cases who have FS examination of no MI or benign findings, FH was MI < 50% (44.4%). Sensitivity, specificity, PPV and NPV of FS for the detection of ≥50% MI goes as follows: 76.3%, 96.4%, 95.7%, and 79.1%, respectively.

Conclusion: With regard to detect depth of MI, FS is useful with high level of PPV. However its lower value of NPV should be considered.
PROGNOSTIC FACTORS FOR PATIENTS WITH FIGO 2008 STAGE I ENDOMETRIAL CANCER

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Objectives: To investigate the prognostic factors for patients with FIGO 2008 stage I endometrial cancer.

Methods: 181 patients were diagnosed as stage I endometrioid adenocarcinoma from 2004 to 2010 at our hospital. 141 patients underwent total hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy. To determine prognostic factors for those patients, histopathological parameters were evaluated by multivariate analysis (Cox proportion hazard model).

Results:
1. A total of 141 patients were identified, 111 (79%) were stage IA, 30 (21%) were stage IB. Cumulative 3 years disease-free survival rate were 93.4% with stage IA and 95.2% with stage IB (p>0.05). 27 patients received adjuvant chemotherapy and one patient was adjuvant radiotherapy. 7 patients (5.0%) recurred and 2 patients (1.4%) died.

2. 6 patients of stage IA and one of stage IB recurred. Recurrence were located in local site (vaginal stump) and in distal sites (lung, paraaortic lymph node, liver, and omentum). Disease free interval was 4-29 months.

3. Positive peritoneal cytology (p=0.026) and lymphovascular invasion (LVI) (p=0.037) were selected as independent significant poor prognostic factors for recurrence compared with other histopathologic parameters (grade, depth of myometrial invasion, and cervical invasion).

Conclusion: Positive peritoneal cytology and LVI were significant poor prognostic factors of stage I endometrioid adenocarcinoma.
Poster Session III

THE CLINICAL VALUE OF INTRAOPERATIVE ASSESSMENTS IN THE MANAGEMENT OF ENDOMETRIAL CANCER

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Objective: The adaptation of lymphadenectomy for endometrial cancer is equivocal. In our center, lymphadenectomy for endometrial cancer is decided from frozen-section results. We investigate the diagnostic accuracy of preoperative assessment and frozen-section analysis (FSA) in endometrial cancer by comparing postoperative histopathology to confirm the usefulness of intraoperative assessment.

Method: A total of 376 consecutive patients with endometrial cancer were included in this study. Histological grade and subtypes, myometrial invasion were investigated with MRI and curettage for preoperative assessments. In FSA, histological grade and subtype, depth of myometrial invasion, lymphovascular space invasion (LVI) were investigated. These results were compared with final histopathology. Data were statistically analyzed.

Results: The accuracy of preoperative examination was 55.6% for myometrial invasion and 59.8% for histological type. In the frozen section, the accuracies of myometrial invasion and histological type were 82.1% and 74.2%. From this results, FSA was superior than preoperative examination (P < 0.001, chisquare test). Our surgical method were suitably performed for 317 patients from postoperative histopathology, 264 of them (83.0%) could be done by using FSA at that time.

Conclusions: We decide the adaptation of lymphadenectomy for endometrial cancer from frozen-section results (Table 1).

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* TAH+BSO was performed for all patients.
TAH: total abdominal hysterectomy  BSO: bilateral salpingo-oophorectomy
PLA: pelvic lymphadenectomy  PALA: paraaortic lymphadenectomy
others: carcinosarcoma, serous/clear adenocarcinoma etc
In endometrial cancer, intraoperative assessment is useful for the adaptation of lymphadenectomy.
Poster Session III

PACLITAXEL PLUS CARBOPLATIN FOR ADVANCED OR RECURRENT CARCINOSARCOMA OF THE UTERUS IN JAPAN

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Purpose: Paclitaxel and carboplatin (PC) have been shown to have activity in carcinosarcoma of the uterus (CS). Ifosfamide and paclitaxel is presently the standard comparator arm for Gynecologic Oncology Group studies; however, its severe toxicity, multiday schedule, and limited activity prompted ongoing investigation for alternate regimens. The purpose of this prospective multi-institutional study was to determine the RR, PFS and OS, and to assess the toxicity of PC in CS.

Patients and methods: We conducted a phase II study of paclitaxel 175 mg/m² plus carboplatin (AUC = 6), every three weeks, until disease progression or adverse effects prohibited further therapy. Eligible patients had histologically confirmed, advanced stage (III or IV), persistent or recurrent measurable disease, and no prior chemotherapy.

Results: Six patients were enrolled between February 2006 and April 2009. The median age of the patients was 61 years; one patient was stage III (17%) and five were stage IVB (83%). Three patients (1; stage IIIC and 2; IVB) received total abdominal hysterectomy plus bilateral salpingo-oophorectomy (50%) as part of the initial treatment; five (83%) had homologous tumors and one (17%) had a heterologous tumor. The median cycle number administered was 4.8 (range: 2-7). RR was 66.7% (2; CR, 2; PR); PFS was 9.1 months. The frequently observed grade 4 toxicities were neutropenia seen in three (50%). Manageable neutropenic sepsis developed in one patient.

Conclusion: The results of this prospective study are the first in Asia showing that PC may be effective and tolerable for advanced or recurrent CS.
Poster Session III

UTERINE LEIOMYSARCOMA DIFFERENTIATION TO RHABDOMYSARCOMA, TREATMENT DIFFICULTIES. A CASE REPORT AND A REVIEW OF THE LITERATURE

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Introduction: Uterine sarcomas are rare mesodermal tumors that account for approximately 3% of uterine cancers, and they usually have a poor prognosis. Uterine leiomyosarcomas and rhabdomyosarcomas may display a great deal of overlap in their morphologic features. Differential diagnosis includes rhabdomyosarcomatous differentiation from leiomyosarcoma and it complicates treatment and prognosis.

Case report: We report a case of a 46-year-old premenopausal woman diagnosed with abdominal fullness and pain of 3 months duration. Ultrasonography showed 15cm uterine mass. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and lymph node biopsy. No extraterine disease was grossly evident but abdominal washing was positive for malignant cells. Stage 3A leiomyosarcoma was diagnosed. Postoperative 6 cycles of doxorubicin, ifosphamide and mesna chemotherapy was given. After 3 months patient developed 10cm intraabdominal mass between spleen and stomach which was positive for 18F-FDG in PET CT. Secondary surgery was performed. Transverse colon and diaphragm had been invaded. Pathologic evaluation showed pleomorphic rhabdomyosarcoma.

Conclusion: Pleomorphic rhabdomyosarcoma is a rare highly aggressive, rapidly progressive tumor with a high case-fatality rate. Morphologic differentiation makes diagnosis and treatment harder. No residual disease at surgery is the most important prognostic factor in sarcoma. The survival benefit of additional lymphadenectomy is still unclear. There are no consensus on adjuvant radiotherapy or chemotherapy. Adjuvant therapy had little effect on survival and 70% of patients died of disease in a mean time of 12 months. These case reports require further clinical studies about treatment in patients with complicated morphologic types of sarcoma.
Poster Session III

SERUM TUMOR MARKERS AS PREDICTIVE FACTORS FOR PROLONGED SURVIVAL IN UTERINE CARCINOSARCOMA

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Background and aims: Uterine carcinosarcoma (CS), also known as malignant mixed müllerian tumor, is one of the most aggressive types of uterine cancer. Purpose of this study was to determine the prognostic value of preoperative serum tumor markers, various clinicohistological factors and treatment modalities in the survival of these patients.

Methods: This is a retrospective study of uterine sarcoma patients, from January 2000 to December 2007. Demographic characteristics such as age, body mass index, parity, smoking, preoperative serum tumor markers (CA-125, CEA, CA 19-9 and CA 15-3), pathological features including stage, grade, myometrial invasion, lymphovascular involvement, epithelial components histological type were collected. Treatment modalities such as type of surgery and administration or not of adjuvant therapy were also recorded.

Results: A total of 37 patients with mean age 68.1 years (SD=10.7 years), participated in the study. The mean follow-up period was 3.5 years (SD = 3.0, range 0.3-12.5 years). Twenty two patients died (62.2%) from disease and one patient (2.7%) died from other causes. When multiple Cox regression analysis with stepwise approach was implied indicated stage as the only significant factor for the outcome. The cumulative event-free rates for one, two and five years were 91% (SE=6%), 78% (SE=9%) and 60% (SE=10%) for cases staged from IA to IIB and 36% (SE=13%), 21% (SE=11%) and 14% (SE=9%) for cases staged from IIIA to IV, respectively.

Conclusions: Our results confirm that early stage of the disease at diagnosis is the only independent prognostic factor for prolonged survival.
Poster Session III

PROGNOSTIC RISK FACTORS FOR LYMPH NODE INVOLVEMENT IN ENDOMETRIAL CANCER PATIENTS

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Objectives: It is difficult to pre-operatively identify the lymph node (LN) involvement because of the uncontrollable variables of change in final pathology. In this study we aimed to analysis the variables affecting LN involvement and to assess the need for systematic lymphadenectomy in endometrial cancer patients.

Methods: A single centre retrospective analysis was performed including patients treated for endometrial cancer between 2009 and 2012. A total of 128 cases were identified. Mann-Whitney, chi-square and Fisher exact tests were used for univariate comparisons when appropriate. Variables with a p value < 0.05 in univariate analysis were included into the logistic regression analysis.

Results: When univariate analysis was performed, histologic grade 2-3, tumour size ≥3cm, myometrial invasion ≥1/2, presence of cervical, adnexial or omental invasion, positive peritoneal cytology, operative technique (laparotomy vs laparoscopy), comprehensive staging (pelvic and para-aortic node dissection vs only pelvic node dissection) and number of pelvic and para-aortic LN removed (>30) were found to be correlate with LN involvement. Together with this when multivariate analysis were performed in regards to predict LN involvement, the number of pelvic and para-aortic LN removed (>30) was found to be the only independent variable that reaches statistically significance [adjusted odds ratio (95%CI) 15.08 (P=0.03)].

Conclusion: Number of pelvic and para-aortic lymph nodes removed (>30) was found to be the only independent predictor of LN metastasis in the study population. Aggressive comprehensive surgical staging including pelvic and para-aortic node dissection should be strongly considered in all endometrial cancer patients.
Poster Session III

EARLY DETECTION OF ENDOMETRIAL PATHOLOGY IN POSTMENOPAUSAL WOMEN USING TRANSVAGINAL ULTRASONOGRAPHY

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Background and aims: To investigate the worth of transvaginal ultrasound in early detection of endometrial pathology.

Material and methods: 94 postmenopausal women were examined. From them 27 with uterine bleeding and normal endometrial ultrasound image; 42, only with pathologic ultrasound image and 26 with both pathologic findings. As pathologic endometrial ultrasound images were considered the endometrial thickness above 4 mm, with irregular structure, polyps and fluid in the uterine cavity. All patients underwent fractioned endometrial curretage followed by histopathological examination of the taken material.

Results: Endometrial cancer was found in 2 cases in the first group, 1 in the second and 5 in the third group. The cancer was most oftenly recognized and proved in endometrial hyperplasia with irregular non-homogenous endometrial structure (19% ), and sporadically found in cases with uterine cavity fluid (3%).

Conclusion: The transvaginal ultrasound is a valuable method in early detection of endometrial pathology in postmenopausal women and can serve as a screening method in selecting patients for invasive diagnostic procedures.
PROGNOSTIC MARKERS AND OUTCOME OF UTERINE AND OVARIAN CARCINOSARCOMA: A FRENCH RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Uterine and ovarian carcinosarcoma are rare forms of gynaecological sarcomas and consequently informations regarding prognostic are scarce. The aim of this study was to describe prognostic of this cancer and to find out independent prognostic factors.

Methods: Retrospective observational study conducted in a French Cancer Centre. Were included all adult women diagnosed with uterine or ovarian carcinosarcoma between January 1993 and January 2012. Overall survival (OS) and disease free survival (DFS) were evaluated. Independent prognostic factors were identified using Cox proportional hazard models where OS and DFS respectively were variables of interest.

Results: Among the 1686 women registered for uterine and ovarian cancer, 69 (59 uterine and 9 ovarian) were diagnosed with carcinosarcoma and included in the study. Median age was of 69 years (IQR 63-77). Median follow-up was 24.2 months (IQR 13.5-54.6). Median OS was 27.1 months (IQR 14.5-72) and median DFS was 21.9 months (IQR 7.9-22.3). pFIGO Stage I represented 28 (41%) patients, while stage II to IV 40 (59%) patients. 33 (49%) tumours were diagnosed autologous histological type and 29 (43%) heterologous. Two factors were found to be associated with death: homologous histological subtype of carcinosarcoma HR=3(95%CI[1.44-6.3]) and high tumor burden (pFIGO stage II-IV) HR=2.64(95%CI [1.29-5.42]). The factors associated with DFS have been evaluated and will be reported at the congress.

Conclusion: Uterine and ovarian carcinosarcomas are specific by the presence of two histological subtypes. Our study suggests that patients with heterologous histological subtype may be associated with good outcome.
CORRELATION BETWEEN PREOPERATIVE BIOPSY, FROZEN SECTION AND FINAL HISTOLOGY IN TYPE 2 ENDOMETRIAL CANCER
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Introduction: Accurate preoperative identification of uterine papillary serous (UPSC), clear cell (ECC) carcinomas and carcinosarcomas (CS) is desirable given that initial treatment recommendations differ compared to those for endometrioid carcinomas (EEC).

Aim: To evaluate the correspondence between preoperative endometrial biopsies, frozen sections and final pathological records in type 2 EC, focusing on their role on subsequent surgery.

Methods: Subjects with type 2 EC of the uterus were identified between the years of 2002 and 2011 at the Mauriziano Umberto I Hospital of Turin. Preoperative procedures such as US, CT, MRI and biopsies were investigated. Data on surgical staging and histological records were collected.

Results: Fortyfour cases (6.5%) of type 2 EC on 670 cases of endometrial neoplasm were identified: 23 were UPSC, 11 ECC and 10 CS.In 37 patients a preoperative biopsy was achieved using: office vacuum aspiration (7 cases), dilatation and curettage of the endometrial cavity (19 cases), hysteroscopy with biopsy (11 cases).Correspondence with the final histological diagnosis was found in 23 cases (62%).In the 14 cases where correspondence was not found with the final report of the pathologists, 2 were undifferentiated (G3) and 12 EEC at preoperative biopsy; an adequate surgical staging was performed in 35% of cases. Frozen section were performed in 14 cases. Correspondence with the final histological diagnosis was found in the 64% of cases, in the remaining cases an undifferentiated carcinoma was found.

Conclusion: A more accurate preoperative identification of UPSC, ECC and CS is desirable to permit a better surgical staging.
NUMB: A NEW PROTEIN IMPLICATED IN THE OCCURRENCE OF ENDOMETRIUM CANCER
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Background and aims: The cell fate determinant Numb orchestrates many cell physiological and pathological processes. An elegant number of evidences have shown the close relationship between numb and tumors. Here, we also want to know whether Numb might also play a vital role in endometrium cancer (EC), which has never been reported.

Methods: We have examined the expression of Numb with immunochemistry method, including in both of normal endometrium tissue and cancer tissue. We also determined the protein levels of Numb with Western blotting and confocal microscopy in cell lines, including EC cell line (HEC-1B) and other the normal epithelium cells. At last, we examined the intracellular location of numb in HEC-1B with confocal microscopy method.

Results: It was showed the higher expression of Numb in EC, compared with the normal endometrium. In addition, we found the Numb accumulated in the nuclear of HEC-B cells, compared with other normal epithelium cells.

Conclusion: Our data suggested that the high expression of Numb in EC was related to the occurrence of EC. At the same time, we firstly proposed it is the translocation into nucleus of Numb that might be the reason for the occurrence of EC induced by high expression of Numb, combining with some previous findings that supported the point of over expressed Numb occurring translocation into nucleus. All together, the truth on roles of Numb in cancer is far from what we have known and needs to be explored deeply.
Poster Session III

UTILIZATION AND EFFECTIVENESS OF INTENSITY MODULATED RADIATION THERAPY FOR UTERINE CANCER

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Background: While intensity-modulated radiation therapy (IMRT) allows more precise radiation planning, the technology is substantially more costly than conformal radiation and to date, the benefits for uterine cancer are not well defined. We examined the use of IMRT and the effect of IMRT on late toxicity for uterine cancer.

Methods: Women with uterine cancer treated from 2001-2007 and recorded in the Surveillance, Epidemiology, and End Results-Medicare database were examined. Use and predictors of IMRT use were examined. The incidence of late-radiation toxicity (gastrointestinal and genitourinary strictures and fistulas, radiation enteritis) and hip fractures were compared for IMRT and conformal radiation.

Results: A total of 3711 patients including 344 (9.3%) who had IMRT were identified. Use of IMRT increased from 1.4% in 2001 to 23.5% in 2007. In a multivariable model year of diagnosis was the strongest predictor of IMRT use (p<0.0001). Demographic characteristics, tumor histology and stage had no effect on receipt of IMRT (p=NS). Women who received chemotherapy (OR=1.68; 95% CI, 1.31-2.15) were more likely to receive IMRT. Compared to women residing in the Eastern U.S., those in the Midwest and West more often received IMRT (p< 0.05). Serious late radiation effects were noted in 597 (17.7%) patients who received conformal radiation and 54 (15.7%) who received IMRT (p=0.34). Hip fractures occurred in 11.7% of the conformal radiation group compared to 10.5% of the IMRT cohort (p=0.49).

Conclusion: Use of IMRT is increasing rapidly. IMRT is not associated with a reduction in late-radiation toxicity or hip fractures.
Poster Session III

DIAGNOSTIC ACCURACY OF 3-DIMENSIONAL POWER DOPPLER ULTRASOUND, MAGNETIC RESONANCE IMAGES AND POSITRON EMISSION TOMOGRAPHY IN PREOPERATIVE IMPRESSION OF UTERINE SARCOMAS

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Aims: To assess the preoperative diagnostic accuracy of sequential use of three different image tools in diagnosis of uterine sarcoma or malignancy involving myometrium.

Methods: Institutional review board approval and informed consent were obtained. From April 2006 to March 2009, 24 consecutive female patients (mean age, 51 years; range, 32-81 years) with suspicion of uterine sarcoma preoperatively who fulfilled the inclusion criteria were enrolled for 3-demensional power Doppler ultrasound (3-D echo), magnetic resonance imaging (MRI) and ¹⁸F-positron emission tomography/computed tomography (PET/CT). Diagnostic efficacy (sensitivity and specificity) and predictive values (positive and negative predictive values) were evaluated for this algorithm. The Receiver operating characteristic curve was used to verify the optimal cut-off points of scores.

Results: Of twenty four patients enrolled for suspected uterine sarcoma, 15 were benign uterine tumors, one smooth muscle tumor of uncertain malignant potential, 2 malignant mixed mullerian tumors, 3 leiomyosarcomas, and three other malignancies involving uterus. The accuracy of 3-D echo, MRI or PET/CT to detect uterine malignancy is 71.4%, 63.6% or 70.8%, respectively. When combined these diverse diagnostic tools, the accuracy reaches to excellent level. The accuracy of both ultrasound and MRI is 85.7%, and both MRI and PET/CT is 90.5%, and both ultrasound and PET/CT is 90.5%. The accuracy of utilizing all these three image tools is also 91.7%.

Conclusions: The preoperative diagnosis of uterine sarcoma is still a challenge for clinician. Using 3-D ultrasound or MRI, and selected PET/CT scan followed by could provide satisfactory diagnostic efficacy preoperatively for predicting uterine sarcoma.
Poster Session III

A STUDY OF JAPANESE ELDERLY PATIENTS WITH UTERINE ENDOMETRIAL CANCER: CLINICAL BACKGROUND AND OUTCOME


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Background: In step with the aging of the population, elderly patients who has uterine endometrial cancer are increasing in Japan. However, there have been few reports concerning special problems on the cancer therapy for elderly person.

Objective: To analyze clinical background and therapeutic outcome in elderly patients with uterine endometrial cancer.

Patients and methods: Ninety-one women with uterine endometrial cancer treated in our institution between 2008 and 2010 are included in this study. To clarify therapeutic special problem on elderly patients, we made a comparison between younger group (< 69 years old) and elderly group (>70 years old). Symptoms, comorbidities before treatment, clinical stage, histopathological classification, treatment options, operative procedures, postoperative complications, postoperative therapies, and clinical outcomes.

Results: There are no difference between younger and elderly group in chief complaint, comorbidities before treatment, clinical staging, complications after the surgical therapy and histopathological finding. On the other hand, there was a tendency to select the surgery without lymphadenectomy in the elderly group. In the elder group, there are no difference in disease-free survival between radical surgery with lymphadenectomy and surgery without lymphadenectomy. However, there were no patients with remission in patients with irradiation therapy.

Conclusion: We should keep in mind that the elderly patients with endometrial cancer had better outcome by surgery even if simple hysterectomy.
Poster Session III

PREGNANCY OUTCOME IN PATIENTS WITH STAGE 1A ENDOMETRIAL ADENOCARCINOMA, WHO CONSERVATIVELY TREATED WITH MEGESTROL ACETATE

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Background: The most effective treatment of well-differentiated endometrial carcinoma is surgery. The aim of this study is the evaluation of megestrol acetate on young patients with well-differentiated endometrial cancer who wish to preserve their fertility, with regard to the receptors.

Methods: 16 patients were treated initially with 160 mg/d of megestrol acetate and continued with 320 mg/d for non-responsive cases. All patients followed with FD&C and hysteroscopy. The responsive patients were referred to IVF group.

Results: Response rate to hormonal therapy was 10/16 (62.5%). The mean time of responding was 7.5 months. Other six (37.5%) patients underwent total abdominal hysterectomy (TAH). Of 10 patients who responded to hormonal therapy, one exited of the study because of her husband’s infertility. Two patients are under IVF. Three patients did not get pregnant and four patients became pregnant and finally underwent TAH. All patients had progesterone receptors. Only one patient lacked estrogen receptors; who also responded to treatment.

Conclusion: Progestins treatment of these patients who want to have child may be useful, but close long-term follow-up is necessary. The evaluation of estrogen and progesterone receptors assay may be useful in predicting response to the treatment.
EVALUATION OF PROGNOSTIC FACTORS IN ENDOMETRIAL CANCER

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Objective: To evaluate of prognostic factors in endometrial cancer, patients with endometrial endometrioid cancer were analyzed.

Patients and methods: Between January 1996 and December 2004, 265 endometrial endometrioid cancer patients were treated. All patients had been performed pelvic lymphadenectomy. Several factors as follows; age (56 years or more), presence of pelvic lymphnode metastasis, myometrial invasion (more than half or not), presence of vessel permeation, positive peritoneal washing cytology, preoperative CA125 value (more than 35U/mL or not), histological grade, and cervical involvement were analyzed.

Results: Univariate analysis showed that presence of pelvic lymphnode metastasis, myometrial invasion (more than half), presence of vessel permeation, CA125 value (more than 35U/mL or not) were statistically significant. A multivariate analysis indicated that only presence of pelvic lymphnode metastasis was independent prognostic factor in endometrial endometrioid cancer patients.

Conclusion: Pre operative evaluation of pelvic lymphnode metastasis in patients with endometrial endometrioid cancer indicates very useful information.
Poster Session III

LOW-GRADE ENDOMETRIAL STROMAL SARCOMA: A RETROSPECTIVE ANALYSIS OF 48 PATIENTS, SINGLE CENTER EXPERIENCE FOR 18 YEARS

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Objective: The aim of this retrospective study was to evaluate the behavior and management outcome of low-grade endometrial stromal sarcoma (LGESS).

Materials and methods: A retrospective analysis was performed involving 48 patients with histologically proven low-grade endometrial stromal sarcoma (LGESS) treated at our institution between 1994 and 2011.

Results: The median age of the 48 patients was 42 years. The most common presenting symptom was abnormal vaginal bleeding. Only 8 patients (17%) were diagnosed with malignancy in our series by preoperative endometrial curettage. With the exception of 2 patients, 46 patients underwent hysterectomy as primary treatment. Twenty patients had adjuvant therapy after the hysterectomy. The median follow-up period was 54 months (range 7-254 months). Fourteen patients (29%) with low-grade ESSs developed disease recurrence, one of whom died from the disease. The median disease-free survival period was 48 months (range 7-197 months). The pelvis (10 cases, 71%) was the most common site of recurrence followed by the lung (7 cases, 50%) and the liver (1 case, 7%). Recurrent disease was treated with surgery (2 cases, 14%), surgery plus chemotherapy (2 cases, 14%), chemotherapy (2 cases, 14%), surgery plus hormone therapy (5 cases, 36%) and only hormone therapy (2 cases, 14%).

Conclusion: The preoperative differential diagnosis of ESSs from other benign gynecologic diseases is often difficult. We recommend adjuvant therapy be administered after hysterectomy in patients with ESS to prevent recurrence or distant metastasis.
Poster Session III

UTERINE ANGIOMYOLIPOMA WITH METASTASIS TO PELVIC LYMPH NODE IN WOMAN WITH TUBEROUS SCLEROSIS: CASE REPORT

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Extrarenal angiomyolipomas (AML) have been reported at various anatomical sites, such as the liver, spleen, abdominal wall, retroperitoneum, oral cavity, penis, spermatic cord, skin, and lung, but infrequently in the gynecological region. In the uterus, only a few cases have been described. We describe a uterine angiomyolipoma occurring in a 41-year-old woman with evidence of tuberous sclerosis. The initial interpretation of imaging pictures and pathologic findings led to the conclusion of myoma but with following successful laparoscopic surgical staging served the diagnosis turned out to be angiomyolipoma in the end. There is no solid data to suggest that usefulness and risk of laparoscopic surgical diagnosis with these tumors until now. So we briefly review the implementtion of laparoscopic surgical diagnosis on angiomyolipoma.
Poster Session III

PROGESTIN THERAPY OF ENDOMETRIAL CANCER IN YOUNG WOMEN AND THE PRELIMINARY STUDY ON RISK FACTORS OF RECURRENCE

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Introduction: Endometrial cancer is one of the most common gynecologic tumors, of which almost 5% patients are younger than 40 years. Progestin has been used as an effective fertility-preserving approach.

Objectives: To evaluate the effect of progestin therapy on early endometroid carcinoma (EC) and to investigate potential clinical risk factors of recurrence.

Patients and methods: From January 2002 to April 2012, forty-one young patients (< 40 years) with intramucous EC treated with progestin as primary therapy in Peking Union Medical College Hospital were retrospectively reviewed.

Results: The overall complete response rate was 87% in a median time of 5.6 months (range 3-12 months). Twenty-six patients desired to conceive after complete remission. Ten women (38.5%) achieved pregnancies, 7 of which had 9 live births. Twenty-four patients had been followed-up more than 12 months (range 12-102 months). Eight patients (33.3%) recurred in 8-48 months (median, 22.6 months). Single Variable Cox Regression was used to seek potential risk factors of recurrence: obesity (OR 0.25, p=0.24) and polycystic ovary syndrome (PCOS) (OR 0.29, p=0.27) might decrease the risk of recurrence; onset of irregular vaginal bleeding (OR 3.12, p=0.33) might increase the risk. However, there is no significant difference. IVF-ET (OR 1.65) and pregnancy (OR 0.67) weren't associated with the recurrence.

Conclusions: Progestin therapy is an optional management to preserve fertility for early EC patients. IVF-ET and pregnancy weren't associated with the recurrence of this disease. Large sample clinical trial is needed to further study other factors like obesity, PCOS or irregular vaginal bleeding.
Poster Session III

LAPAROSCOPIC SURGERY FOR TREATMENT OF PATIENTS WITH ENDOMETRIAL CANCER

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Background and aims: The traditional approach for the treatment of endometrial cancer by laparotomy is increasingly being replaced by laparoscopic surgery. The advantages of laparoscopy have been well-documented. Laparoscopy avoids the morbidity of a laparotomy, overcomes the limitations of vaginal hysterectomy, provides adequate pathological information for an accurate surgical staging and expedites the postoperative recovery of patients. Here reports the outcome of a series of 56 consecutive cases of endometrial cancers which were performed laparoscopic hysterectomy and pelvic and para-aortic lymphadenectomy by the author. The objective is to review the perioperative, postoperative experience and survival outcomes of patients with endometrial cancer managed by laparoscopic surgery performed by a single surgeon.

Methods: The records of 56 consecutive patients with endometrial cancers from May 2010 to March 2012 treated by laparoscopic pelvic lymphadenectomy and laparoscopic hysterectomy were retrospectively reviewed. Data on patients' attributes, endometrial cancers, surgical procedures, surgical complications and morbidity, perioperative experience, length of hospital stays and clinical outcome were analysed.

Results: Laparoscopic surgery was successful in all 56 patients. The mean operating time was 186 minutes (standard deviation, 16 minutes) and the mean operative blood loss was 50 mL (standard deviation, 10 mL). The mean hospital stay was 7 days (standard deviation, 3.5 days). The intra-operative and postoperative complication rate was 3.6%, including bleeding, small lymphocyst.

Conclusions: Obviously laparoscopic surgery is an option for the treatment of early endometrial cancer. Careful patient selection and surgical competency are key factors to ensure successful treatment.
Poster Session III

A COHORT STUDY EVULATING PARAAORTIC LYMPHADENECTOMY IN ENDOMETRIAL CANCER IN CHINA

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Objective: To assess the role of paraaortic lymphadenectomy (LNE) in women with endometrial cancer.

Method: We analyzed patients diagnosed with endometrial cancer, staging from IA to II preoperatively. Inclusion criteria is without preoperative adjuvant therapy and were performed hysterectomy plus systematic pelvic LNE and paraaortic LNE by laparoscopy or laparotomy.

Result: 54 patients who underwent surgery for preoperative endometrial cancer were identified. LNE was performed in all the patients. Pelvic and paraaortic lymph node metastases were identified as 11.1% (6/54) and 7.4% (4/54), with total lymph node positive rate is 14.8% (8/54). Blood loss, operating time, lymph node count and status showed no statistical significance between two surgical pathways. And laparoscopy relates with shorter postoperative inhospitalization days and recovery days.

Conclusion: Our results show the high rate of metastasis to pelvic and paraaortic lymph node of the endometrial cancer which alert us the importance of the systematic LNE, especially paraaortic lymph node, for endometrial cancers. And no severe complication is caused by LNE besides lymph cyst. In sum, it is necessary to perform LNE, especially no neglecting of paraaortic lymph node, so as to reach better post-operative therapy. And laparoscopy manifests similar surgical effects as laparotomy, but gains much advantage over it.